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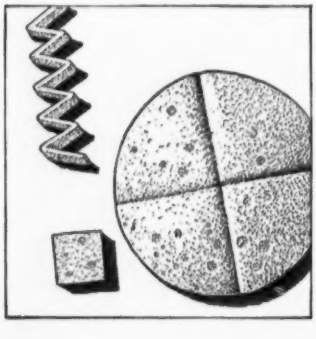

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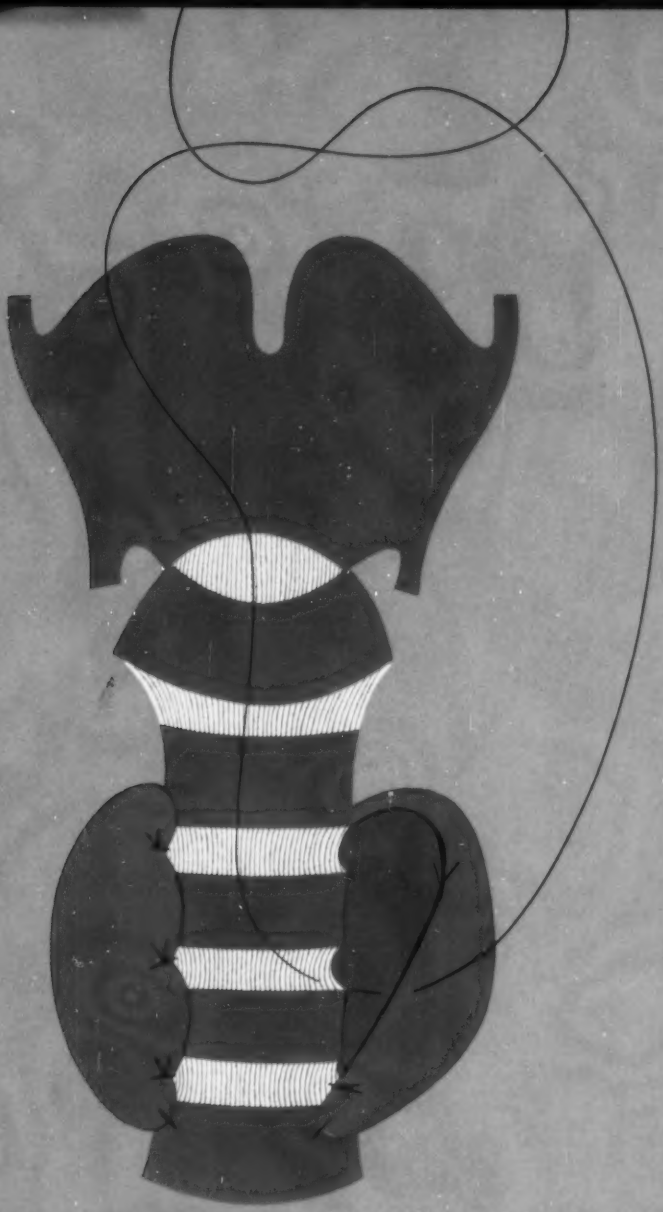

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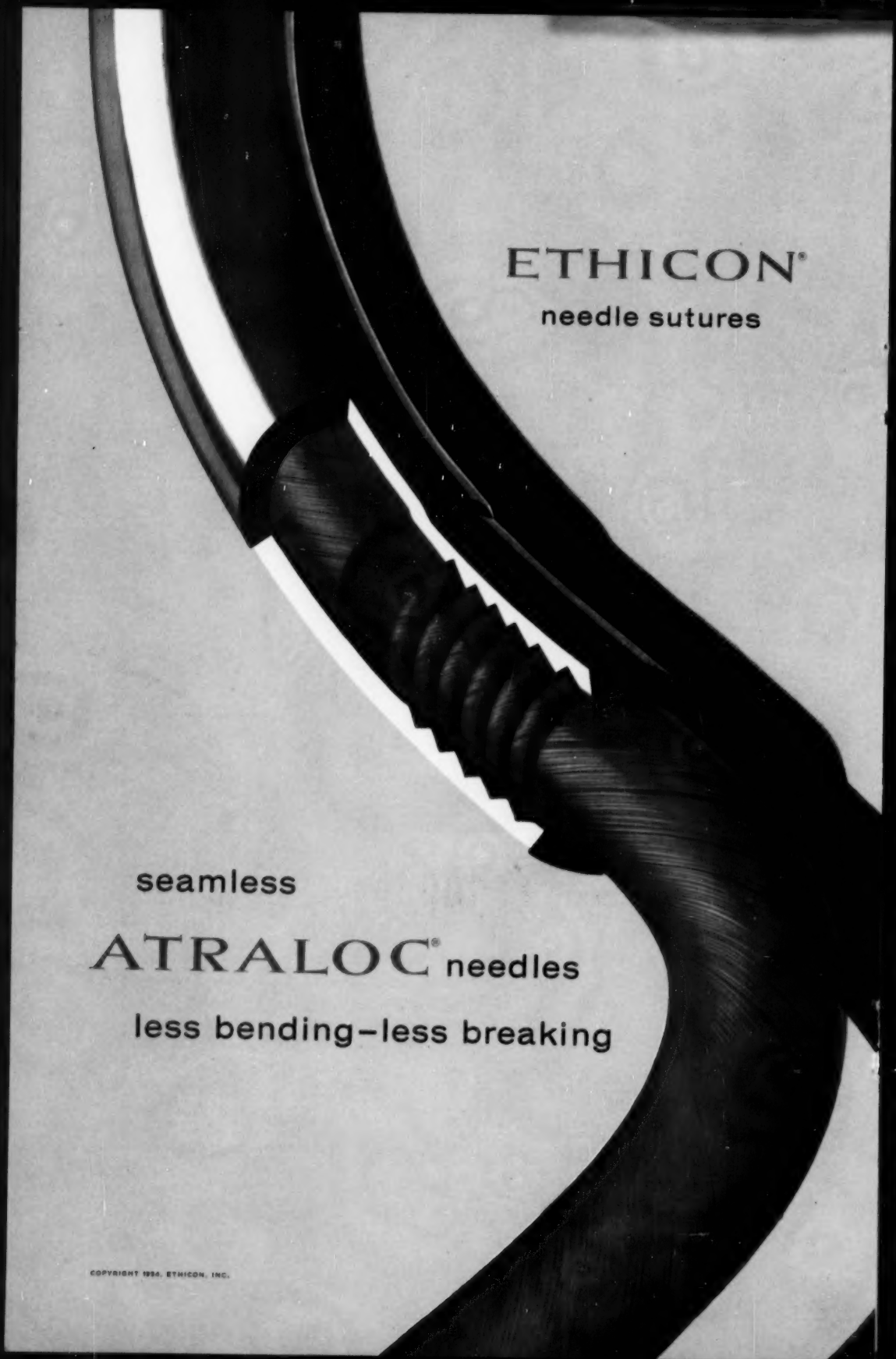

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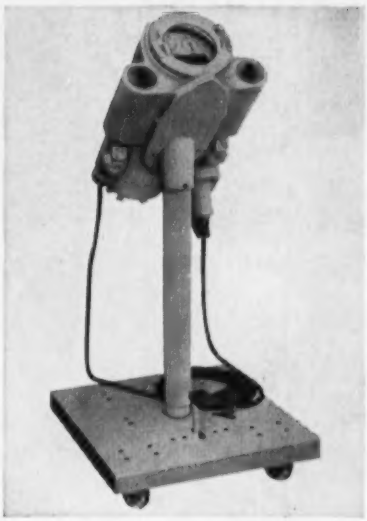

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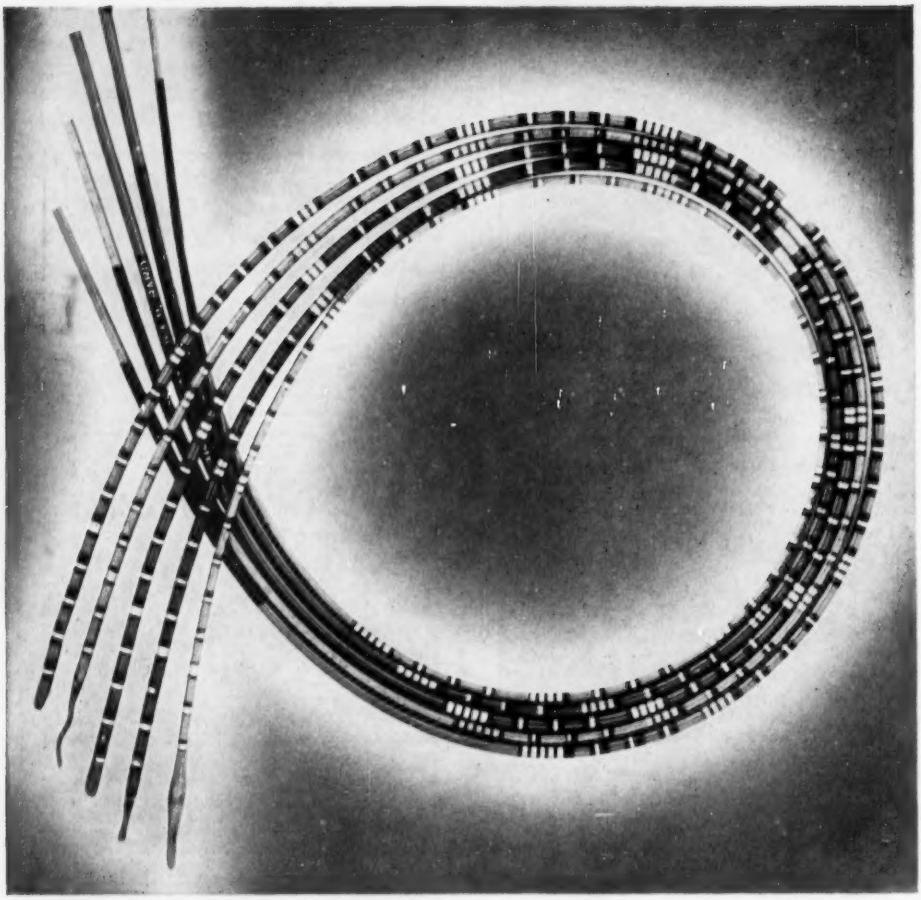

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VOLUME 69 SEPTEMBER 1954 NUMBER 3

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SELECTION OF PATIENTS FOR MITRAL COMMISSUROTOMY IN RELATION TO CLINICAL RESULTS

ORMAND C. JULIAN, M.D.
WILLIAM S. DYE, M.D.
AND
WILLIAM J. GROVE, M.D.
CHICAGO

SURGICAL separation of the cohered leaflets of the stenotic mitral valve has become established as a satisfactory operation.* As an application of a new principle, it has from the earliest reports by Bailey † provided a relatively constant and high proportion of good clinical results. Aside from minor variations, some of which are undoubtedly improvements, there has been little change in the technical aspects of mitral commissurotomy. Although, with greater experience, the safety and the anatomical thoroughness of the procedure have improved, there has been little real change in the percentage of good results. This, however, has not been a matter of wide dissatisfaction because of the continuous, rather high proportion of good results and because of the realization that certain aspects of the disease process prevent more accurate preoperative prediction of what commissurotomy will do for individual patients.

Selection of patients as it is generally done cannot fully cover all the features of the disease which in the end will determine the result of operation. Selection depends upon certain requirements involving the patient's stage of disability and a consideration of certain contraindications. It is generally accepted that although patients should be operated upon early in the course of the disease, certain significant symptoms should be present. At this point, the selection of patients for surgery by classification fails to take adequately into consideration the pathology of the disease. Identical anatomical pathologic features of the stenotic mitral valve, such as size of the opening, age of the process, and consistency of the scar, may be present in a patient showing the earliest manifestations of the disease as are present in a patient showing intractable right heart failure. Reference to this fact has been made frequently, and this is simply a reminder that the anatomical result of rheumatic fever on the mitral valve is by no means the only factor responsible for symptoms in mitral stenosis. The other aspects of the disease which are involved are the degree of damage sustained by the myocardium, particularly of the right ventricle, during the rheumatic episode and whatever effective changes have occurred which

Read at the 11th Annual Meeting of the Central Surgical Association, Detroit, Feb. 19, 1954.

From the Department of Surgery, University of Illinois College of Medicine, Research and Educational Hospitals, and the Cardiovascular Service, St. Luke's Hospital, Chicago, and the Vascular Service, Veterans Administration Hospital, Hines, Ill.

* References 1 to 4.

† References 5 and 6.

in general determine the respiratory efficiency of the lungs.[7] Some dissatisfaction then may be expressed on this end of the disease scale in that selection by classification alone fails to offer surgery to certain patients whose clinical manifestations are now considered to be too meager to justify this treatment. Selection of these patients for surgery from others who manifest only a murmur as a sign of their disease will depend on x-ray demonstration of an increased right heart work-load and on catheterization studies which demonstrate increased pulmonary pressure and diminished ability to increase cardiac output during work.

Failure to achieve a rising rate of benefit in patients with Grade II and Grade III disease probably has two causes. One is the incorrect evaluation of the importance of involvement of other valves by the rheumatic process and of the degree of insufficiency which coexists with the mitral stenosis. The second cause of failure to improve statistics depends upon an inability to determine externally the structural nature of the mitral stenosis. This is a particularly serious disadvantage because there seems to be little hope of improving diagnostic acumen to a degree which would provide information on this minute but most important point. Although in Stage IV the same failure to progress from the standpoint of bettering results of surgery may be pointed out, it would seem that the approach of most surgeons in these cases has been correct. If other valvular malformations and irreversible pulmonary changes can be excluded as major causes for the poor cardiac state of these patients, commissurotomy, with a full understanding of the dangers and disappointments, has been generally recommended.

It is determined primarily that the patient's symptomatology meets the requirement for surgery, on the one hand, and, on the other, that the degree of pulmonary vascular change does not contraindicate surgery. All other items of judgment as to the operability of a patient with this valvular affliction depend upon evaluation of the prime responsibility of mitral stenosis for the patient's condition.

History is an aid in this determination on several points. It is extremely rare, as found in our series, that manifestations of peripheral congestion precede symptoms of pulmonary inadequacy. Patients with mitral stenosis have, in our experience, had a recognizable progression of symptoms. Dyspnea on exertion as a primary symptom has been almost universal and is frequently accompanied by the complaint of rapid heart rate or palpitation with exertion. These early symptoms have been widely judged to be on the basis of an inability of the heart to increase its stroke volume and output because of the mitral constriction. As the mitral stenosis results in a progressively greater degree of pulmonary hypertension, the dyspnea routinely is accompanied by a cough and attacks of pulmonary edema and by paroxysmal nocturnal dyspnea. Hemoptysis is an evidence of the effect of pulmonary hypertension, either because of capillary rupture or because of pulmonary infarction which may be produced (usually on a small scale) by pulmonary vascular thrombosis secondary to the hypertension and stasis. These stages are followed in the history, in patients with more advanced disease, by the manifestations of the inability of right heart to maintain the high work-load demanded of it. Increased peripheral venous pressure, enlargement of the liver, ascites, and dependent edema are the outward results. Acute pulmonary infection in the early stages of pulmonary hypertension may produce a rapid progression to manifestations of right heart failure. On the whole, however, signs of right heart failure preceding pulmonary signs are

strongly suggestive that severe myocardial weakness due to rheumatic fever is present or that valve lesions other than mitral stenosis are playing a significant part in the patient's disability.

The finding of a rumbling middiastolic and presystolic murmur at the cardiac apex is rarely absent in mitral stenosis.[8] The addition of murmurs other than this characteristic one brings about greater difficulty in evaluation of an individual patient for surgery. Basilar diastolic murmurs result from an accompanying aortic insufficiency secondary to high pulmonic artery pressure and relative dilatation of the pulmonary orifice. Systolic apical murmurs may or may not be an indication of a significant anatomical mitral regurgitation. It is common experience that in the presence of a systolic apical murmur surgery may disclose either a mitral valve which is principally regurgitant or one in which a tiny remaining orifice in the stenotic valve is held open by the rigidity of the cusps or a valve in which no reflux during ventricular systole occurs. Finally, of the additional murmurs in mitral stenosis, the systolic murmur in the aortic valve area, having a cervical radiation, requires evaluation.

TABLE 1.—*Results*

Stage	Exc.	Good	Unchanged	Worse	Dead
II	3	4	0	0	2
III	25	43	9	5	9
IV	6	14	3	3	13
Total	34	61	12	8	24
	95 (68.3%)		20 (14.4%)		(17.3%)

When the murmurs of aortic insufficiency, mitral insufficiency, and aortic stenosis are of real functional importance in the patient's cardiac condition, they are expected to show an accompanying effect of hypertrophy or dilatation of the left ventricle.

RESULTS OF STUDY

The present study is based upon the pre and postoperative evaluation of 139 patients, of whom 78 were female and 61, males. Statistics involving operative and surgical mortality are based on a total of 160 patients. Of this original 160 patients, 21 have been lost to follow-up or have been operated upon too recently for postoperative evaluation. Study of the results in relation to factors which influence the original selection of these patients for surgery has been carried out in an attempt to develop criteria for future selection. The study covers a three-year period from January, 1951, through January, 1954. Ninety-five of the surviving patients have been followed six months or longer. Of these patients, 65 have been followed longer than one year. All patients have been followed for at least two months postoperatively. In the 139 patients comprising this study, the result of surgery was judged to be excellent or good on objective evidence in 95 patients and unchanged or worse in 20 patients. Seven postoperative deaths occurred. Seventeen of this series represent the late mortality (death after leaving hospital). The objective results are given in Table 1, which also divides the data into that obtained at various stages in the cardiac disease. The groups mentioned refer to the classification of the New York Heart Association of 1939.[9]

The result of commissurotomy upon the 132 patients remaining after the surgical mortality of 7 has been judged objectively on the basis of all available criteria. These criteria are relief of orthopnea and freedom from attacks of failure, improvement or relief of dyspnea and cardiac palpitation, true weight gain, reduction in heart size by x-rays, ability to discontinue medication, and occasionally on the basis of electrocardiographic changes toward improvement when it was significantly disturbed preoperatively. Of nine patients in Group II that were operated upon, seven showed significant and valuable improvement, and two were dead. These deaths are both late deaths, as shown in Table 5, and both followed a significant period of good improvement. No satisfactory explanation for either of these deaths is available. In Stage III, which accounts for 91 of the patients operated upon, 68 patients so classified are significantly improved, while 14 are unchanged or worse since surgery. Nine of these patients have died. Thirty-nine Group IV patients have been operated upon. Twenty show excellent or good results. Six are unchanged or worse, and 13 are dead.

In order to evaluate the important point of the influence of such associated valve lesions as aortic disease and mitral insufficiency, the incidence of left heart enlargement in relation to results is shown in Table 2. Certain of the patients reported on

TABLE 2.—*Influence of Left Heart Enlargement on Results*

	Patients, No.	
	Excellent or Good Result	Poor Result
Left heart enlargement	14	21
No left heart enlargement	88	3

in Table 2 are now dead. However, they had lived for a length of time sufficient to judge their result as excellent, good, unchanged, or worse. Therefore the total number of patients reported on in Table 2 exceeds the total number of patients now living. This portion of the study indicates that of 102 patients having excellent or good results, only 14 had enlargement of the left ventricle as judged by x-rays and electrocardiography, while 88 showed no left ventricular enlargement. On the other hand, of the patients who were either unchanged or made worse by surgery, 21 had left ventricular enlargement, while 3 did not show this enlargement. Assuming that left ventricular enlargement follows directly as a result of significant aortic valvular disease or mitral insufficiency, this tabulation represents only a restatement of the principle that these lesions are unfavorable findings from the standpoint of prognosis following surgery. Table 2 illustrates, however, the importance of the presence of functionally pure mitral stenosis in selection of patients.

The meaning of an apical systolic murmur has been subjected to limited study in this series. Table 3 indicates the reliability of this sign in relation to the surgical finding of sufficient regurgitation through the mitral orifice to be felt by the operator's finger within the left atrium. In 60 patients showing a distinct apical systolic murmur, 23 failed to have such a degree of actual regurgitation and 12 who showed no such systolic murmur had a definite regurgitant jet at surgery. This demonstrates a definite unreliability in regard to the physical sign and stresses the importance of left ventricular hypertrophy in discovering patients having a significant degree of regurgitation.

The frequency of an accompanying auricular fibrillation stimulated an evaluation of the meaning of this abnormal rhythm in terms of results. Table 4 shows the correlation of results with the presence or absence of auricular fibrillation prior to and during surgery. The majority of our patients were in auricular fibrillation during the surgical phase—86 with fibrillation and 48 without fibrillation. Of those with fibrillation, 54 patients obtained an excellent or improved state as a result of surgery, 11 were the same or made worse, and 21 are dead. Of those without fibrillation, 39 were improved or excellent, 6 were the same or worse following surgery, and 3 are dead. In percentages, 60% of those with fibrillation and 83% of those without fibrillation benefited from surgery, while 24% of those with fibrillation and 6% of those without fibrillation have died subsequent to surgery. The mortality in patients in auricular fibrillation at the time of surgery is not unexpected, although considered by itself, it would seem to be an unexpectedly serious criterion. When the mortality is evaluated on the basis of the patients' clinical grouping, as in Table 5, the true meaning of fibrillation as simply an accompaniment of the more serious stages of the disease is made evident.

TABLE 3.—*Correlation of Apical Systolic Murmur with Palpable Regurgitant Jet**

	Patients with Murmur Present, No.	Patients with no Murmur, No.
Jet present	37	12
No jet	23	52

* In 89 of 124 patients, correlation present; in 35 of 124 patients, no correlation.

TABLE 4.—*Correlation of Results with Fibrillation at Time of Surgery*

	Patients, No.			
	Excellent or Improved	Same or Worse	Dead	Total
Fibrillating	54	11	21	86
Not fibrillating	39	6	3	48

TABLE 5.—*Mortality*

Stage	Operative (100 patients)	Late (139 patients)
II	0	2
III	3	6
IV	4	9
Total	7 (4.6%)	17 (12.1%)

Total mortality 17.3% (139 patients)

An attempt was made to evaluate, in the light of results, any data which might indicate that the patient continued to have some rheumatic infection. Four of the 139 patients followed showed a serious postoperative episode of fever and pleuropericardial pain of the type described by others who suggest that this syndrome represents a recurrence of rheumatic fever. In two of these four patients, results have been good to excellent. Of the other two, one is a late mortality and one is

unchanged or worse. Four additional patients showed late febrile episodes not associated with pulmonary, renal, or other explanation. One of these displayed a migratory rheumatoid arthritis, and all were considered to have rheumatic recurrences. In these patients whose postoperative course suggested rheumatic fever, preoperative manifestations were not recorded. Although the sedimentation rate was elevated sporadically throughout the series in other patients, these did not show a positive result in this test.

Some comparison between the results as judged by the patients themselves and the results evaluated clinically can be seen by comparing Table 7, which relates the patient's opinion of his operation, with Table 1. Seventy-six patients responded to a questionnaire with answers that were sufficiently definite for reliable interpretation. Eight-six per cent of the patients responding said that they were benefited to an excellent degree, while 14% said that they were the same or worse than they were before surgery. The percentage of patients evaluating their result as being poor is identical with the percentage so judged on the basis of objective examination.

TABLE 6.—*Incidence of Emboli (160 Patients)*

		Nonfatal		
	Fatal	Transient	Persistent	Total
Peripheral	1	..	..	1
Cerebral	3	2	3	8
	4 (2.5%)			9 (5.6%)

TABLE 7.—*Results as Judged by Patient*

Patients Questioned, No.	Patients Responding, No.	Results			
		Normal	Improved	Same	Worse
100	76	21	44	7	4
		65 (86%)		11 (14%)	

The percentage judging themselves to be significantly improved is quite a bit higher than the figure obtained by objective means. This discrepancy could be on the basis of bias in that there might be a tendency on the part of the patients not benefiting by surgery to be more anxious to make this fact known in the sense of a complaint. It may also be explained on the basis of the psychological effect on a chronically ill cardiac patient of a surgical procedure which he has undergone. This comparison cannot be offered as a significant result of the study. It is, however, a strong suggestion that any study based to a large extent on the patient's opinion of his result may be subject to error.

The complication of peripheral arterial emboli occurred in nine patients of the total series of 160. A summary of the results of this complication is given in Table 6. In one of the nine patients the embolus, which was fatal, was peripheral, while in eight the embolus was cerebral. Of the three cerebral emboli that were fatal, one occurred on the fifth postoperative day; the other two occurred on the day of surgery. Two patients with cerebral emboli have recovered completely. The overall incidence of emboli in this series has been 5.6%. Fatal emboli occurred in 2.5% of the patients.

MORTALITY

There has been no operative mortality as a result of technical accident or abnormal cardiac rhythm during the surgical procedure. There have been seven in-hospital deaths, accounting for 4.6% of the total number of patients operated upon. This is based upon a total of 160 operations for mitral stenosis, including two cases in which commissurotomy was not actually done. One of these patients was found to be inoperable on the basis of a complete encasement of the atrial cavity in thrombus, and the second was considered inoperable because of palpable evidence through the atrial wall of total mitral regurgitation. Five patients have been lost to follow-up, and 16 (not including any deaths) have been operated upon too recently to include in figures relating to results. These are therefore not included in the total calculation of the delayed mortality. Seventeen patients have died since leaving the hospital. These represent 12.1% of the 139 patients used as a basis.

COMMENT

The lack of mortality due to technical difficulties or to serious cardiac arrhythmias demonstrates the general safety of the procedure in all classes of patients. Negation of this sense of security, however, is shown by the incidence of cerebral embolism, which, although it occurred at the time of surgery, did not produce death until later in the postoperative period. The complication of peripheral arterial and cerebral arterial embolism continues to be a shortcoming of the surgical procedure. It is apparent from our results that the gross finding of clots within the atrium or its appendage is not a reliable indication of danger of this complication. Tourniquet compression of the subclavian and carotid arteries as practiced by Bailey has not been utilized in our series. Compression of the carotid artery by the anesthetist during parts of many of the procedures has been done, with results which cannot be evaluated. Recently, a more direct approach has been instituted in those cases discovered at surgery to have interauricular clots which are not densely and firmly adherent to the wall. A suction tube attached to a powerful suction machine has been introduced alongside the index finger which has discovered the clots. The tube is clamped during introduction. It is brought into proximity or contact with the thrombus and the suction released. In one rather spectacular case in which this technique was applied, a large firm clot was heard to engage in the tube end and instantly pass through the suction outfit. It was found later in fragmented form in the suction bottle. Future improvement in mitral valve surgery may possibly be looked for when, under direct vision accomplished with hibernation or pump, the atrial wall may be sucked clean of all thrombi before the valve is opened by careful cutting under vision.

In relation to the total mortality in any series of such cardiac operations, it is to be remembered that, in time, the late mortality will become 100%. Even when operated upon early in the course of the disease, these patients with their excellent results remain cardiac patients in some degree, and, as such, are not free of fatal sequelae later on. It is expected, therefore, that the total over-all mortality (i. e. deaths in the hospital and deaths subsequent to discharge) in this series of 17.3% will increase, although the constant addition of patients newly operated on will continue to have the opposite effect.

SUMMARY

The study of the objective results obtained in 139 operations for mitral stenosis has shown benefit of a lasting nature to a significant proportion of patients. The importance of left heart enlargement as related to prognosis after mitral commissurotomy is reemphasized. The observation that an apical systolic murmur is not always reliable evidence of functional regurgitation further emphasizes the importance of left heart enlargement as a prognostic sign. The operative mortality in the series has been 4.6% with an incidence of fatal peripheral arterial emboli of 2.5%. The total mortality was 17.3%. There have been no deaths from technical difficulties or serious cardiac arrhythmias.

Nineteen of the total deaths reported occurred in 39 Group IV patients operated upon. We believe elimination of Group IV as operative candidates because of high mortality would not be justified in view of 20 good or excellent results produced in such patients.

DISCUSSION

Dr. Conrad R. Lam, Detroit: Dr. Julian and his group are to be congratulated on this rather large series of mitral stenosis cases and the results they have obtained.

In giving this discussion, I can almost use the transcript of the remarks I made two years ago in Toronto on Dr. Julian's paper. I mentioned a very good test to see whether or not there is complicated mitral stenosis, which is the simplest imaginable, and that is merely to look at the patient. The very first thing we like to do in seeing a new patient with mitral stenosis is to view the chest completely undraped. If the precordium is very still, as if there were no heart beat, it is a good indication that pure mitral stenosis is present. If there is a great deal of precordial activity, it is almost sure to be due to left ventricular hypertrophy.

There is one other thing which needs to be added at this time, and that is that the prognosis is not now so bad even if there is some left ventricular hypertrophy because it may be due to aortic stenosis.

I should like to diverge from the subject just long enough to say that Bailey's method of treatment of aortic stenosis with the dilator is very successful—even better than Dr. Bailey indicates—and if both lesions are present, one can do the two commissurotomies at the same time with good results.

Dr. E. H. Fell, Chicago: Dr. Grove discussed very well the main points in selecting patients for mitral commissurotomy. I should like to emphasize that patients with valvular heart disease with left ventricular hypertrophy, as shown by x-rays and electrocardiographic studies, should not be treated for mitral stenosis. A mitral stenotic valve that causes increased pulmonary artery pressure is accompanied by right ventricular hypertrophy, and patients that have these findings, with a good myocardial reserve, have a good prognosis following surgery.

We believe, as Drs. Julian, Dye, and Grove, that patients with right ventricular hypertrophy and evidence of left ventricular hypertrophy of less degree than the right ventricular findings indicate, do not have as good a prognosis as those with right ventricular hypertrophy alone, because the mixed ventricular hypertrophies mean associated mitral regurgitation, aortic disease of considerable degree, or both.

We believe that a patient with mitral stenosis as the main cause of disability and with pathology of other valves (aortic or pulmonary) of less degree should be given the opportunity of surgical benefit derived from opening the mitral commissures. We have seen definite benefit in this group. The patient and relative should be informed that the patient is not an ideal candidate for the procedure, and that the risk is greater and the results not as happy. The risk is worth taking, and the majority will be relieved so that they can care for themselves.

Dr. William J. Grove, Chicago: I agree with Dr. Fell that right ventricular hypertrophy is an essential sign for the diagnosis of symptomatic mitral stenosis. Its demonstration by x-rays is much easier than left ventricular hypertrophy. However, when left ventricular hypertrophy can be demonstrated, it is a poor prognostic sign.

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CONGENITAL ABSENCE OF HEMIDIAPHRAGM AND USE OF A LOBE OF LIVER IN ITS SURGICAL CORRECTION

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CONGENITAL diaphragmatic hernia per se constitutes a threat to life in the newborn. If an operation is not performed, according to available statistics, most of these infants do not live beyond two months. The most serious of these defects is the complete absence of the hemidiaphragm. No report of an operative survival for the correction of this abnormality was found in a review of the American and British literature. It is the purpose of this paper to describe a new operative technique which has been successfully executed in man. Subsequent clinical experience and animal experiments make it appear that this is a reasonable approach to the problem. The technique involves the suture of the respective lobe of the liver to the endothoracic fascia to separate completely the thoracic and abdominal cavities. If it becomes necessary to resect a large portion of the diaphragm because of malignant growth, it is felt that this same technique may be applicable.

In a newborn showing cyanosis and dyspnea or vomiting, diaphragmatic hernia should be considered. Cyanosis may be evident immediately after delivery, or it may be transient and appear only when the baby is crying or eating. It may be so severe that oxygen therapy is constantly required to sustain life. Physical examination of these infants usually shows a rapid respiratory rate and a heart that is displaced away from the affected side. Auscultation may reveal absent or distant breath sounds and intestinal gurgles if peristalsis has begun. Roentgenological examination of the chest will show the heart and mediastinal structures displaced to the unaffected side, and possibly suspicious gas shadows in the affected side. The insertion of a small stomach tube and the introduction of either thin barium or iodized oil (Lipiodol) will definitely prove the diagnosis.

Diaphragmatic defects can be classified into six main categories:

1. Hernia through the foramen of Bochdalek (pleuroperitoneal canal)
2. Large posterior diaphragmatic defects (no attachments of the posterior diaphragm to the chest wall; deficiency of the diaphragmatic leaf)
3. Esophageal hiatus hernia
4. Hernia through the foramen of Morgagni
5. Congenital absence of the hemidiaphragm

Read at the 11th Annual Meeting of the Central Surgical Association, Detroit, Feb. 19, 1954.

From the Western Reserve University School of Medicine, Department of Surgery at City Hospital.

Congenital absence of the hemidiaphragm fortunately is not common but, of course, does offer the gravest prognosis. Our experiences with two cases outline the numerous problems involved.

REPORT OF CASES

CASE 1.—A 6 lb. 13 oz. (3,090 gm.) white baby girl was delivered normally at St. Alexis Hospital at 3:35 p. m., on Oct. 10, 1952. Respirations were spontaneous, but immediately it was noted that they were labored and the baby was cyanotic. Physical examination revealed breath sounds to be absent on the left. Atelectasis of the left lung was at first suspected. Laryngoscopy and aspiration of the bronchial tree were done, with no improvement in the general condition of the baby. X-rays of the chest showed the heart to be displaced to the right with no aeration of the left lung (Fig. 1). After this a small catheter was inserted into the stomach and a small

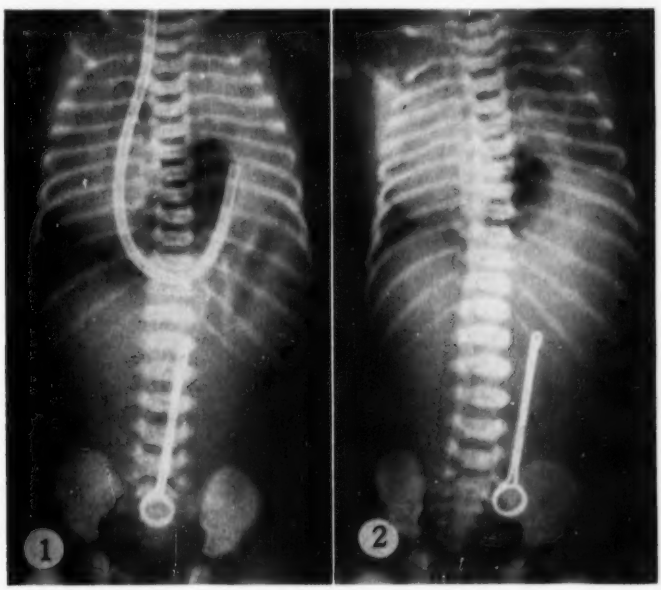

Fig. 1.—Thoracic stomach outlined by the insertion of a small catheter and the introduction of air.

Fig. 2.—Heart displaced into the right thorax. Gas-filled loop of the stomach and intestines fill the left thorax.

amount of air injected. This maneuver demonstrated the stomach to be in the left thorax (Fig. 2). A diagnosis of congenital diaphragmatic hernia was made, and the baby was operated upon on Oct. 12, 1952, approximately 48 hours after delivery, when adequate intravenous fluid and electrolyte therapy had been accomplished.

With the use of endotracheal anesthesia the baby was placed in the oblique position with the left side propped up at approximately a 45 degree angle. A skin incision was made in the abdomen midway between the xiphoid and the umbilicus and continued laterally up along the left eighth interspace. The abdomen was opened and explored. When it was found that all of the abdominal organs, with the exception of the kidneys, descending colon, and rectum, were in the left thorax, the pleural cavity was entered. By gentle traction the colon, small intestines, stomach, spleen, and finally the liver were placed in the abdomen. The left hemidiaphragm was completely absent. The left lobe of the liver fell naturally into position, separating the abdominal and thoracic

cavities. It appeared that the liver might serve as an effective diaphragm. For this reason it was sutured to the endothoracic fascia with interrupted 000 nonabsorbable surgical (silk) sutures on Atraumatic needles. Upon completion of the suture line posteriorly and laterally, the right leaf of the diaphragm was sutured to the liver along the medial aspect. The chest wall was closed by placing pericostal and intercostal sutures through the liver, thus effectively separating the abdomen from the pleural cavity. A No. 14 Foley catheter was placed in the left thorax for drainage. Repeated efforts during surgery to expand the left lung were unsuccessful. At the time of the closure the left lung was still completely collapsed against the mediastinum. In spite of this, the baby's condition at the conclusion of the operation was much improved (Fig. 3).

Postoperatively the baby was placed in an incubator; continuous gastric suction was instituted, and the thoracotomy tube was attached to underwater suction. Administration of penicillin, 200,000 units, and streptomycin, 0.1 gm., which had been started a short time after birth was continued every 12 hours. Intravenous fluids were given very slowly through a polyethylene intravenous catheter.

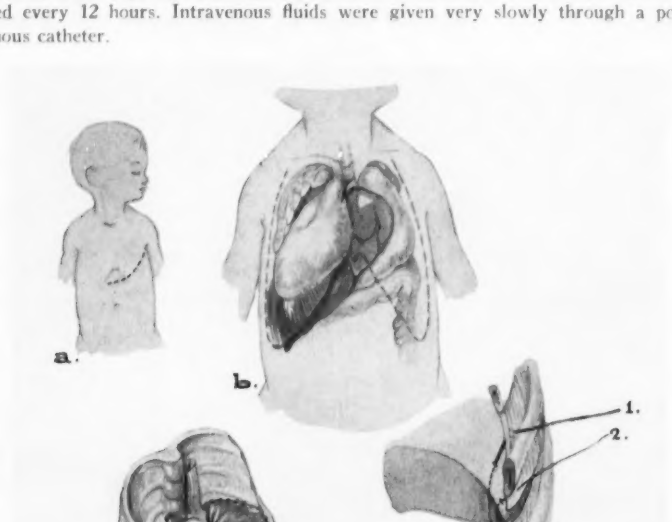

Fig. 3.—(*a*) Baby in the oblique position. A thoracoabdominal incision was made. (*b*) All of the abdominal organs except the right lobe of the liver and the descending colon were in the left chest. Heart displaced into the right thorax. (*c*) Edge of the liver sutured to the endothoracic fascia with interrupted silk sutures. (*d*) Pericostal and intercostal sutures inserted through the liver.

During the first 48 hours the baby's respirations were shallow and labored, accompanied by intermittent cyanosis. Her temperature remained near 103 F. rectally. Frequent tracheal aspirations were necessary, and her respirations gradually became much deeper. Negative pressure was applied to the thoracotomy tube every four hours, blood-tinged fluid being removed. Gradual expansion of the left lung took place, and in two weeks the baby could be left out of the incubator without becoming cyanotic. The thoracotomy tube was removed on the ninth postoperative day, when x-rays of the chest showed the heart to be back in its normal position and both lungs to be aerating well (Fig. 4).

Oral feedings begun on the third postoperative day were tolerated poorly for two weeks. The baby was discharged on Nov. 11, 1952, weighing 6 lb. 14 oz. (3,118 gm.).

Recent x-rays of the stomach show a rather high position of the newly created diaphragm, but on crying there is no further ascent of this structure and no herniation (Fig. 5). There is

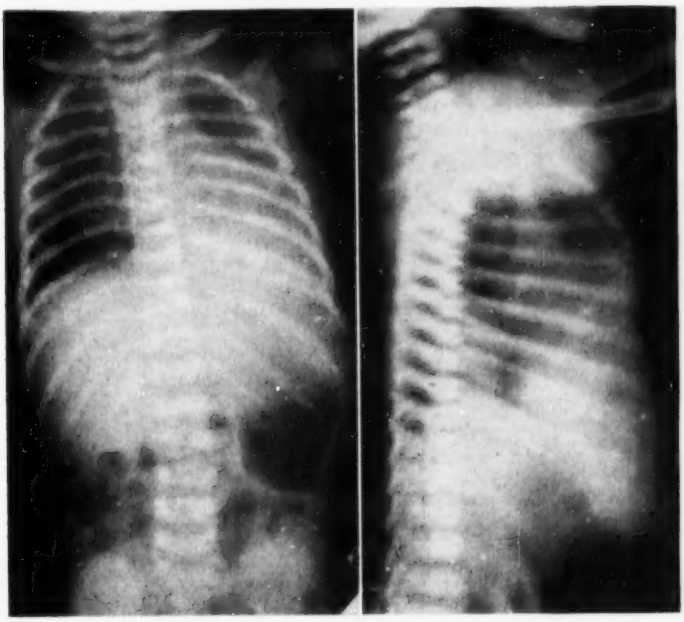

Fig. 4.—X-rays of the chest, taken at one month. Heart is in the midline.

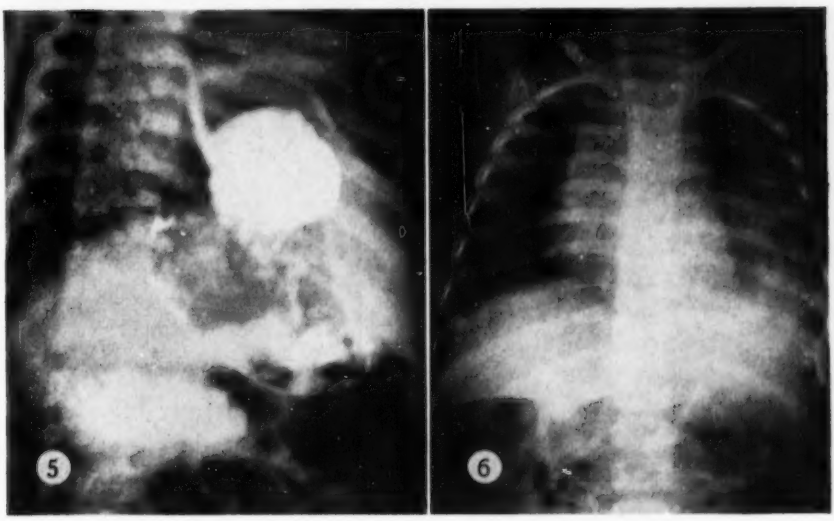

Fig. 5.—High position of the liver diaphragm. No evidence of herniation.
Fig. 6.—X-rays of the chest taken at 18 months of age.

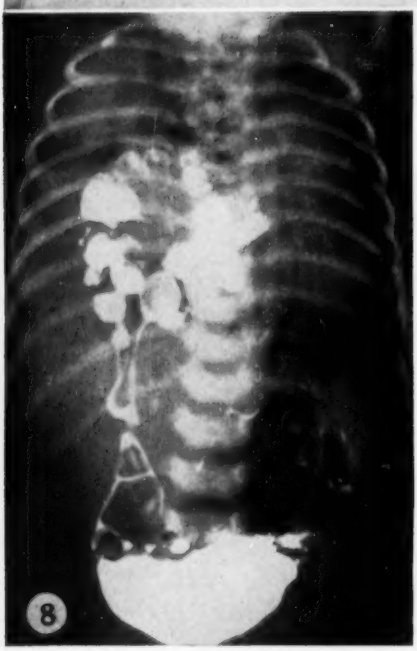

Fig. 7.—Photograph of patient at 18 months of age.
Fig. 8.—Stomach is in the abdomen. Barium-filled intestine herniated into the right thorax.

no evidence of paradoxical motion of the chest wall. The stomach, although dilated, empties completely in three hours. Cephalin flocculation and sulfobromophthalein retention are normal, as is a urinary urobilinogen. At the present time she is in good health without respiratory or circulatory embarrassment. Digestive symptoms have not been manifest (Fig. 6).

CASE 2.—In December, 1952, Baby H., a 24-hour-old, seven and one-half month premature infant, with the classic signs and symptoms of right diaphragmatic hernia, was delivered at Huron Road Hospital. X-rays showed the stomach to be in the abdomen, but the small bowel and most of the colon were in the right thorax (Figs. 7 and 8).

With the use of endotracheal anesthesia an incision was made into the abdominal cavity. The right hemidiaphragm was found to be completely absent, and the incision was continued along the eighth intercostal space. The colon and small intestine were moderately distended, and some difficulty was experienced in reducing them. An attempt was made to suture the liver to the endothoracic fascia. Because of the marked intestinal distention sutures cut through the edge of the liver. Inspection revealed that the prerenal fascia could be reflected. This fascia was sutured loosely anteriorly and laterally to the endothoracic fascia, thus partially separating the abdominal and thoracic cavities. Then the liver was sutured to the prerenal and endothoracic fascias, effectively creating a barrier between the two cavities. The right lung was completely atelectatic and proved impossible to expand. The anterior closure of the thorax was essentially the same as that of Case 1. At the conclusion of the operation, cardiac arrest occurred, which failed to respond to cardiac massage and other measures. A complete autopsy disclosed no other abnormalities.

EXPERIMENTAL OBSERVATIONS

To investigate the technique further, healthy mongrel dogs were anesthetized with intravenous pentobarbital sodium (Nembutal), 30 mg. per kilogram of body weight. Through a thoracoabdominal incision under aseptic conditions, the hemidiaphragm on the respective side was resected in its entirety. The corresponding lobe of the liver was sutured to the endothoracic fascia with interrupted 000 silk on Atraumatic needles. The sutures were placed through the parietal pleural and endothoracic fascia and then deeply through the edge of the liver. Medially the opposite leaf of the diaphragm was sutured to the liver. Pericostal sutures of 0 silk were passed through the substance of the liver before being brought out around the lower rib. Intercostal sutures of fine black silk were similarly placed. The intercostal sutures held the liver firmly against the chest wall to prevent subsequent disruption. After the operation, 500,000 units of penicillin was given subcutaneously and for the first few postoperative days. Air was aspirated from the thorax with a large needle and syringe before the intratracheal tube was removed.

In seven animals the right hemidiaphragm was resected. The left was similarly treated in seven others, while in two, both sides of the diaphragm were completely removed. In each instance the liver was used to repair the defect by the technique described.

Four of the dogs died in the immediate postoperative period. Of the early postoperative deaths, two were the result of technical errors. The inferior vena cava was partially transected during preliminary resection of the right hemidiaphragm in one instance. The second animal died as the result of a left atelectasis and pleural effusion resulting from the placement of intermediate lobe of the liver in the chest above our suture line. The other two fatalities resulted from a rupture of the suture line following gastric dilatations. This included one animal in which both sides of the diaphragm had been resected. The survivors were killed from two weeks to a year following operation. Immediate autopsies revealed the livers to be densely fused to the parietal pleura and difficult to disrupt manually (Fig. 9). A firm, dense fibrous sheath completely covered the superior aspect of the liver, and the peripheral portion of the lower lobe was adherent to it. Abdominal inspection revealed no evidence of herniation. Other than atelectasis of the lower lobe of the lung and moderate passive congestion of the liver, histological examination failed to reveal other abnormalities.

To test the pressure necessary to disrupt the "liver-diaphragm," the abdominal cavity was subjected to air pressure. At 40 lb. (18 kg.), air suddenly escaped into the thorax. Autopsy of this animal, in which the complete diaphragm had been resected a year previously, revealed that the liver on either side was intact; the disruption occurred in the soft tissue between the sternum and the pericardium. In four animals, dying within 24 to 48 hours following operation, the strength of the new diaphragm was dependent upon the suture line. Fibrous union between the liver and the parietal pleura occurred within three days and appeared to be complete within a week. Observations of the animals revealed no evidence of paradoxical motion of the chest wall on the treated side; however, intercostal breathing was

Fig. 9.—Abdominal aspect of a dog killed three months after a left hemidiaphragmatic replacement with the liver.

prominent. Complete intercostal breathing was observed when both diaphragms were replaced by the liver.

Cephalin flocculations and sulfobromophthalein liver function tests were performed on the blood of five dogs. In all instances the cephalin flocculation tests were reported as 3 to 4+, and in three, the sulfobromophthalein retention was elevated.

COMMENT

There is an erroneous impression that newborn infants do not stand major surgical procedures. As a result, operations for congenital defects of the diaphragm are withheld until the infant is at the point of death from respiratory and circulatory embarrassment or intestinal obstruction.[2] Only recently, repair of congenital dia-

phragmatic hernia in infancy ceased to carry a high mortality. Hedbloom reported a mortality rate of 75% in 1925.[11] Up to the time when Orr and Neff reviewed the literature in 1936, they found only 17 infants under one year of age who had been operated upon for this defect. They added one successful case of their own. The mortality in this group of 17 infants was 47%. Hartzell,[10] Ladd and Gross,[12] Donovan,[4] and Gross [8] in 1946 reported mortality rates from operations ranging from 24 to 50%. Harrington, in his most recent article, reported 7 deaths in a group of 25 newborn infants operated upon with the diagnosis of congenital diaphragmatic hernia.[9] Tolins in a recent review of the literature states that 75 children under one year of age have been operated upon successfully, adding a case of his own.[17]

The closure of most diaphragmatic defects is simply a matter of approximating free edges. However, in large congenital defects, eventration, diaphragmatic resection for primary malignant growths or secondary to pulmonary or abdominal malignant lesions, closure may be impossible without an alternate procedure. Such alternatives have involved mobilization of the renal fascia,[18] interposition of latissimus dorsi muscle, or partial resection of the lower ribs in order to reduce the size of the defect.[3] Cutis grafts have been used experimentally with success and employed by Metheny in a case in which the central tendon of the diaphragm was resected in a total gastrectomy for carcinoma of the stomach.[14] Grindlay and Waugh replaced most of the hemidiaphragm in two dogs with polyvinyl (Ivalon) sponge during their investigation work on the tissue implantation of this material. They were pleased with their results.[7]

It is apparent that a diaphragmatic substitute should be readily available, of good tensile strength, and large enough to cover the defect. The right lobe of the liver completely covers the abdominal aspect of the right hemidiaphragm; hence in a congenital absence or surgical removal it can be sutured to the inside of the thorax or to the remaining edges of the diaphragm. On the left side, the situation is more difficult, for this lobe is much smaller than the right. However, by transecting the falciform ligament, the left lobe can easily be drawn over and sutured to the endothoracic fascia in the manner described.

Clinically and experimentally we have not found bleeding from the liver to be a problem. The fine silk sutures will not cut through the liver substance unless they are tied too tightly. The weakest point in the entire suture line is posteriorly, where the strength of the created diaphragm is entirely dependent on one row of interrupted sutures. Anteriolaterally two separate rows of sutures firmly hold the surface of the liver to the chest wall.

Most of the authors cited believe that an abdominal approach to this defect is adequate.* It is our opinion, on the basis of these clinical and experimental operations, that good exposure and the use of available tissue for repair can be obtained by a thoracoabdominal incision.

Despite rupture of the posterior suture line in four animals, it is apparent that such a situation is less likely to occur clinically where it is possible to employ measures to avert gastric or intestinal postoperative distention. That the liver diaphragm is adequately strong to separate the abdominal and thoracic cavities after healing occurs is demonstrated by the pressure required to rupture it. Similarly, the excel-

* References 5, 9, 13, and 16.

lent postoperative courses of Case 1 and the surviving 12 animals suggest that when healing is completed there is no further tendency for diaphragmatic hernias to occur.

It is suggested that this technique may be applicable when it becomes necessary during the resection of malignant lesions to remove all or part of the diaphragm.

SUMMARY

An operation is described to replace an absent hemidiaphragm by suturing one lobe of the liver in the defect. This procedure has been applied in two infants with congenital absence of a hemidiaphragm. One of these children is now 18 months after operation and in excellent health.

To test this operation, experimental operations were performed on 16 dogs in which one or both leaves of the diaphragm were entirely resected. Four dogs died; the remainder showed excellent healing and no tendency to develop diaphragmatic herniae.

Mr. Howard Peacock gave technical assistance.

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CONGENITAL DIAPHRAGMATIC HERNIA

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DURING the past seven years we have observed 33 cases of congenital diaphragmatic hernias at the Children's Memorial Hospital, 31 of which have undergone surgical repair. During the course of this experience, several important points in the care of these patients have been forcefully impressed upon us.

Congenital diaphragmatic hernias may be classified as follows:

1. Esophageal hiatus hernia
   (*a*) Congenitally short esophagus
   (*b*) True hiatus hernia
2. Hernia through the foramen of Morgagni
3. Hernia through the foramen of Bochdalek
4. Eventration of the diaphragm
5. Congenital absence of the diaphragm

The cases being reported are outlined in the Table, and the occurrence of the hernias in various areas of the diaphragm is illustrated in Figure 1.

CONGENITALLY SHORT ESOPHAGUS

In early fetal life, if the stomach descends incompletely behind the septum transversum and does not reach the abdominal cavity before the lumbar portion of the diaphragm is completed, the esophagus may remain short and a portion of the stomach will stay within the thoracic cavity. Because the shortened esophagus enters the uppermost portion of the stomach, the normal relationship of cardia and fundus is lost.

X-ray examination with a barium or iodized oil swallow will demonstrate the short esophagus and a portion of stomach within the chest (Fig. 2). Esophagoscopy will confirm the transition of esophageal to gastric mucosa well above the level of the diaphragm.

The commonest complication is mucosal ulceration and stricture formation at the gastroesophageal juncture, giving rise to an incomplete obstruction, with symptoms of regurgitation and poor weight gain. These strictures have been treated by our endoscopy department by dilatations with uniformly excellent results.

Only one patient had had narrowing of the esophageal hiatus of such a degree as to necessitate surgery. Partial obstruction at the level of the passage of the stomach through the diaphragm gave symptoms of persistent vomiting of most of the oral intake and finally hematemesis. At the age of 7 days the infant was operated upon by way of a left transthoracic approach. The esophagus was elongated somewhat by extensive mobilization. Then the esophageal hiatal opening could be brought up to the level of the gastroesophageal junction, where it was snugged and sutured

From the Department of Surgery, Children's Memorial Hospital.
Read at the 11th Annual Meeting of the Central Surgical Association, Detroit, Feb. 19, 1954.

Summary of Data *

Case	Age	Symptoms	Operation	Type	Results
1	10 hr.	Oomphalocele	Abdominal	Bochdalek	Cured
2	11 hr.	Dyspnea and cyanosis	Abdominal	Bochdalek	Died
3	18 hr.	Cyanosis	Abdominal	Bochdalek	Cured
4	1 day	Dyspnea	Thoracic	Bochdalek	Died
5	1 day	Dyspnea	Abdominal	Bochdalek	Cured
6	1 day	Dyspnea and cyanosis	Abdominal	Morgagni (sac)	Cured
7	2 days	Dyspnea and cyanosis	Abdominal	Bochdalek	Cured
8	2 days	Dyspnea and cyanosis	Abdominal	Bochdalek	Cured
9	3 days	Dyspnea	Abdominal	Bochdalek	Died
10	3 days	Dyspnea and cyanosis	Abdominal	Bochdalek	Cured
11	3 days	Dyspnea	Abdominal	Bochdalek	Cured
12	4 days	Dyspnea and cyanosis	Abdominal	Bochdalek	Cured
13	4 days	Dyspnea	Abdominal	Bochdalek	Died
14	4 days	Dyspnea, cyanosis, and vomiting	Abdominal	Bochdalek	Cured
15	5 days	Dyspnea and cyanosis	Abdominal	Bochdalek	Cured
16	7 days	Hematemesis	Thoracic	Short. esoph.	Late death
17	12 days	Dyspnea and cyanosis	Abdominal	Bochdalek	Cured
18	19 days	Hematemesis	Thoracic	Esoph. hiatus	Cured
19	24 days	Cyanosis	Abdominal	Bochdalek	Cured
20	2 mo.	Dyspnea with feeding	Thoracic	Eventration	Cured
21	3 mo.	Vomiting	Abdonimal	Midline (sac)	Late death
22	6 mo.	Borborygmi	Thoracic	Esoph. hiatus	Recurrence
23	7 mo.	Vomiting	Thoracic	Bochdalek	Cured
24	7 mo.	None	Thoracic	Bochdalek (sac)	Cured
25	7 mo.	None	None	Eventration	.....
26	11 mo.	Dyspnea and cyanosis	Thoracic	Bochdalek	Cured
27	13 mo.	Constipation	Thoracic	Bochdalek (sac)	Cured
28	14 mo.	None	Thoracic	Eventration	Cured
29	15 mo.	None	None	Esoph. hiatus	.....
30	21 mo.	Cyanosis ±	Thoracic	Bochdalek (sac)	Cured
31	2½ yr.	Recurrence	Thoracic	Bochdalek †	Cured
32	4 yr.	None	Thoracic	Bochdalek (sac)	Cured
33	11 yr.	Cough	Thoracic	Eventration	Cured

* Essential information concerning the cases being reported: Symptoms were severest in the group under 6 days of age. Abdominal surgical approach was used almost exclusively in this early age group, and the herniation, with only one exception, occurred in the foramen of Bochdalek. Symptoms were moderate or absent in the patients over 6 days of age. Thoracic surgical approach was used exclusively in patients over 6 months of age. Cases over 1 year of age all had some type of hernia with a confining sac.

† Case 31 had been operated upon elsewhere at the age of 2 months and therefore symptomatically belongs in the younger age group.

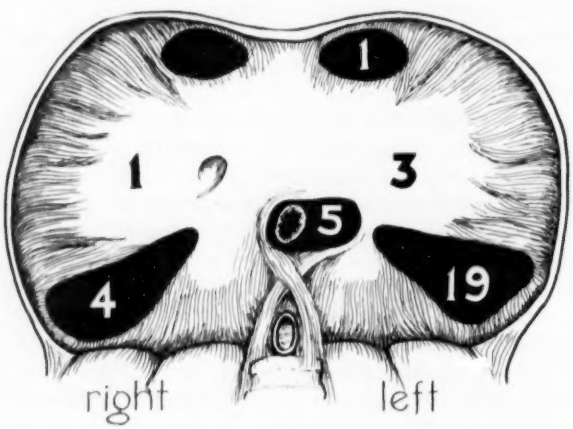


Fig. 1.—Ventral view of diaphragm showing various sites of congenital diaphragmatic hernia. Figures represent the occurrence in each area in the reported series. Numbers on the dome of each diaphragm represent eventration.

to the esophagus with interrupted nonabsorbable surgical (silk) sutures. In spite of successful repair, the patient died one month later of congenital hydronephrosis and other unrelated anomalies. Postoperative x-ray examination had revealed relief of the obstruction, and postmortem examination showed the repair to be intact.

ESOPHAGEAL HIATUS HERNIA

Delay in descent of the stomach from the thoracic cavity to the abdominal cavity may keep the esophageal opening abnormally dilated during development of the diaphragm. Though the stomach eventually reaches its normal abdominal position and the esophagus attains normal length, this weakness in the esophageal hiatus will allow stomach and occasionally other viscera to herniate into the chest. These organs are always contained in a true hernial sac.

The hiatus hernias we have observed in infants have consisted of displacement of the upper portion of the stomach into the chest, including the fundus and cardia. The esophagus is of normal length but is buckled up in the mediastinum into a tortuous channel, as seen on x-ray examination (Fig. 3). These are not the common type of paraesophageal hernias which develop in older patients and in which a knuckle of the fundus herniates alongside a normally placed esophagus.

A hernia of this type rarely becomes symptomatic during infancy and childhood. Of the three cases we have observed, two were incidental findings on routine roentgenograms of the chest. The masses above the left diaphragm were identified by fluoroscopy and barium meal. One of these patients had operative repair, but the other was completely asymptomatic and therefore is being observed only.

The third patient presented an interesting problem.

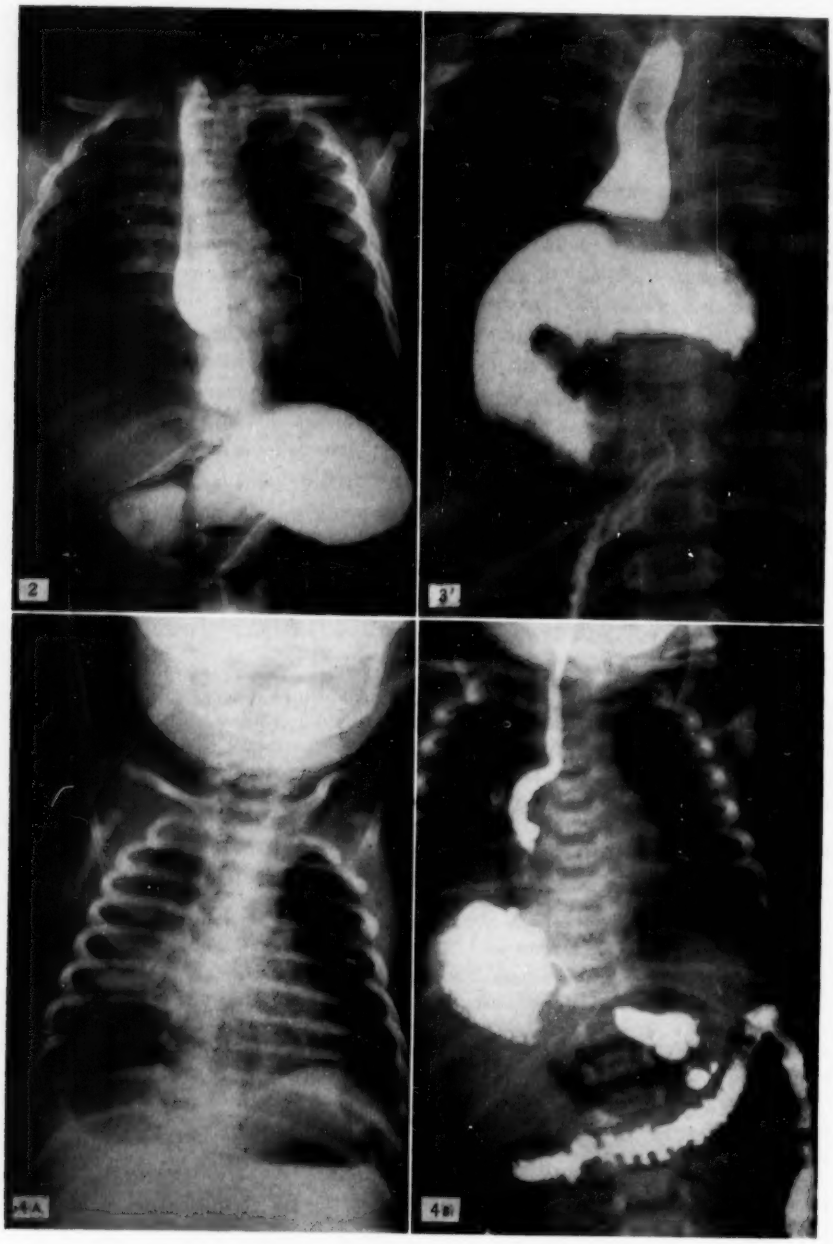
CASE 18.—A 19-day-old white boy entered the hospital with a history of vomiting after each feeding for the previous six days. Examination revealed a dehydrated infant. The abdomen was scaphoid without gastric peristaltic waves. Some observers felt that there might be a mass near the midline of the upper abdomen. The child vomited every feeding, and progressively the vomitus became "coffee ground" in nature.

X-ray examination of the chest revealed a mass in the right lower lung field with an air-fluid level (Fig. 4*A*). Iodized oil given by mouth filled the supradiaphragmatic cavity but did not go below the diaphragm. With pressure, a catheter could be inserted through the esophagus into the stomach below the diaphragm, which was then filled with radiopaque medium through the catheter. (Fig. 4*B*). The preoperative impression was either duplication of the stomach or diaphragmatic hernia with strangulation.

A right thoracotomy was performed. The upper half of the stomach had herniated through a narrow fibrotic esophageal hiatus into the right chest. The esophagus was of normal length and tortuous. The stomach wall was dusky-blue in color and covered with a thin sac. The stomach was replaced in the abdomen, and the esophageal hiatus was snugged about the lower end of the esophagus and sutured to the muscularis to prevent recurrence.

Since the diagnosis of hypertrophic pyloric stenosis had also been entertained, the infant was carefully observed postoperatively. On the second postoperative day barium was given by mouth, and x-rays showed normal position of the stomach but high-grade pyloric obstruction. Three days after the initial operation the abdomen was opened and a typical pyloric tumor was found. Pyloromyotomy was performed, and the patient left the hospital seven days later in excellent condition.

The symptoms this patient presented were the results of the two coexisting conditions. If hypertrophic pyloric stenosis had not developed, the hiatus hernia might have gone unrecognized until later life. On the other hand, if the herniation had



Figures 2 to 4

(See legends on opposite page)

not been present, the patient would have presented the typical course of pyloric stenosis without hematemesis or the confusing roentgenographic picture. Evidently, as obstruction at the pylorus became more complete, the esophageal hiatal opening was unable to accommodate the dilated and hypertrophied stomach and so venous stasis and hematemesis resulted.

In the patient without symptoms, operative repair is not urgent and some authorities believe it is unnecessary. Others contend that it is safer to repair a well-defined esophageal hiatus hernia while it is uncomplicated and the patient is a good surgical risk than to wait until old age, ulceration, hemorrhage, and adhesions render the operation difficult and dangerous.

Although various elaborate procedures may be necessary in the older age group, in infants we have contented ourselves with simple inversion and imbrication of the sac and snugging of the esophageal hiatus.

HERNIA THROUGH THE FORAMEN OF MORGAGNI

Occurrence of herniation through the anterior defect in the foramen of Morgagni, has been explained as a failure of the central and lateral portions of the diaphragm to fuse. The fact that most of these hernias have a true sac confining them suggests that completion of the diaphragm by the layers of a pleuroperitoneal membrane had been accomplished but that growth of the muscle between these two layers had been inadequate in this area, allowing intestines or liver to herniate into the thoracic cavity.

Only one of our patients had a herniation through this region of the diaphragm. As usual, a definite hernial sac was present, but in spite of this confining sac enough of the intestines had crowded into the left chest to produce severe symptoms during the first few hours of life. Diagnosis and treatment are similar to those for hernia of the foramen of Bochdalek and will be discussed below.

HERNIATION THROUGH THE FORAMEN OF BOCHDALEK

The embryology of herniation through the foramen of Bochdalek is somewhat more complicated but can be briefly outlined as follows:

The separation of the common body cavity into the thoracic and abdominal compartments is accomplished by a series of orderly steps during the development of the embryo.

The septum transversum forms beneath the heart and grows backward to meet the dorsal mesentery of the foregut, completing the central portion of the diaphragm.

EXPLANATION OF FIGURES 2 TO 4

Fig. 2.—Barium swallow in a case of congenitally short esophagus. Upper narrowing at level of ninth vertebra represents the entrance of the esophagus into the stomach. Lower constriction is due to passage of the stomach through the diaphragm.

Fig. 3.—X-ray examination of the esophagus and stomach following a barium meal reveals an esophageal hiatus hernia with tortuosity of the esophagus and a portion of the stomach (fundus and cardia) herniating into the left chest.

Fig. 4.—X-ray examination of the chest in Case 18. *A*, an air-filled cavity lies above the right leaf of the diaphragm. *B*, iodized oil given orally fills the cavity above the diaphragm and shows tortuosity of the esophagus. In order to put oil into the stomach below the diaphragm a catheter had to be inserted. Colon fluoroscopy had been noncontributory.

A pleuroperitoneal fold then forms and gradually extends laterally and posteriorly to complete the division of the body cavities. The last portion to be bridged is posterior and is known as the pleuroperitoneal canal, or foramen of Bochdalek. Gradually the layers of pleura and peritoneum close this gap, and muscle fibers derived from cervical myotomes grow between the layers to form the final diaphragm. This is completed between the eighth and ninth week of fetal life. The left side of the diaphragm is completed later than the right, explaining the predominance of hernias on the left.

During formation of the diaphragm the midgut is lying out in the umbilical cord, where rapid elongation and development into its various components is taking place. The intestine returns to the abdominal cavity rather suddenly at about the 10th week of fetal life. Tardy closure of the diaphragm or too early return of the gut to the abdominal cavity may result in a portion of the newly returned intestine finding its way into the pleural cavity through the uncompleted diaphragm. This plug of intestines probably prevents further closure of the diaphragmatic defect, just as the toe of a salesman's shoe keeps the housewife from shutting the door. Entry of the bowel into the pleural cavity before the pleuroperitoneal membrane has covered the defect results in a herniation without a confining sac. However, if the bowel pushes into the thorax after the pleural and peritoneal layers have formed but before muscular tissue has developed, the hernia will have a true sac.

Diagnosis.—At birth the infant may appear to be normal, but as the herniated bowel fills with gas and, later, food, cyanosis and dyspnea become evident. Labored respirations with inspiratory increase in the intrathoracic negative pressure tends to suck more of the abdominal contents into the pleural cavity. Cyanosis and rapid labored respirations then become progressively more alarming so that prompt steps to establish a diagnosis must be taken. Unlike esophageal hiatus hernia, vomiting is rarely a prominent symptom.

Upon examination the cyanosis and extremely rapid respirations will be noted. Respiratory motions are not like those seen in a normal newborn who depends so much on the diaphragmatic component of breathing. There is, instead, an alternate rise and fall of the chest and abdomen, resulting in a rocking type of respiration. The abdomen is usually scaphoid, the degree depending upon the amount of abdominal contents herniated into the chest. Dullness to percussion and decreased breath sounds will be found on the affected side of the chest, while the heart is usually markedly displaced toward the opposite side. Usually repiratory excursion on the affected side will be diminished. The presence of peristaltic bowel sounds over the area of herniation seems to be a highly overrated sign. In a majority of our cases the examiners were unable to hear bowel sounds even though the diagnosis had already been established by x-ray examination. On the other hand, one occasionally hears of cases in which thoracic intestinal peristalsis was thought to be heard, but subsequent x-ray examination or operation proved absence of a diaphragmatic hernia.

Roentgenograms of the chest usually establish the diagnosis. Gas-filled intestinal loops and often stomach will be seen in the thoracic cavity, with collapse of the lung on the affected side and displacement of the mediastinum and its contents to the opposite side (Fig. 5). Lateral view of the chest may help in locating the defect more accurately. Studies of the gastrointestinal tract with barium or even iodized oil

are usually unnecessary and may be harmful. Only in cases in which the diagnosis is obscure and one wishes to rule out lung cysts, staphylococci, pneumonia with multiple air-filled abscess cavities, or a rare duplication of the intestine, is such an examination warranted (Fig. 6).

Treatment.—It has become obvious that surgical correction of this type of congenital diaphragmatic hernia is the treatment of choice and that delay in operation may be fatal.

Preoperative Treatment.—Several things must be done between the time the diagnosis is established and the time of surgery. Passage of a catheter into the stomach and establishment of continuous suction will prevent further gastrointestinal distention and may even accomplish some degree of decompression. Propping the child in a semiupright position and rolled toward the affected side may encourage partial reduction of the hernia and improve respiratory capacity. Oxygen given by tent or into an incubator usually improves the distressing cyanosis and dyspnea.

Anesthesia.—Scopolamine hydrobromide is given before operation to decrease secretions and reduce the amount of anesthetic agent needed. Doses of 1/400 or 1/600 grain (0.15 or 0.10 mg.) are given to the newborn infant. Increase in this amount is based upon the age and condition of the patient. The older child is also given appropriate amounts of morphine.

Endotracheal anesthesia is given to aid in inflation of the lungs. A combination of ether-oxygen or cyclopropane-oxygen were used in all cases.

A piece of polyethylene tubing is inserted into an ankle vein, and intravenous fluids are started so that blood may be given quickly if necessary and postoperative parenteral feedings are facilitated.

Operation.—The route of surgical approach must be the first decision. It has become our policy to use the abdominal approach with this type of hernia if the patient is 6 months of age or less. The factor controlling this decision should actually be an evaluation of the amount of viscera in the chest compared to the potential capacity of the peritoneal cavity rather than an arbitrary age limit. Many patients have required stretching of the abdominal wall to allow closure of the abdominal wound. In two cases primary skin closure alone was all that could be obtained. In another child the abdominal closure was so tight that a partial wound separation occurred postoperatively. In none of these instances could the hernia have been reduced and closure of the defect accomplished through a thoracic approach alone.

A generous abdominal paramedian incision is made on the same side as the hernia. The defect in the diaphragm can be palpated and exposed. The liver is no great problem in right-sided hernias, since it can be partially brought out of the abdomen and dislocated toward the left.

A No. 16 catheter is inserted through the defect into the pleural cavity to allow air to enter as viscera are removed (Fig. 7). The contents of the hernia, bowel, stomach, spleen, liver, etc., can then be withdrawn and laid upon warm, moist pads outside of the abdominal cavity. When the intestines have entered the chest during fetal life immediately upon their return to the abdomen from the umbilical sac, one can expect a lack of normal rotation and attachment. The duodenum, pancreas, and colon may be free of attachments to the posterior abdominal wall. In these cases it may be well to look for and divide any abnormal bands that might later

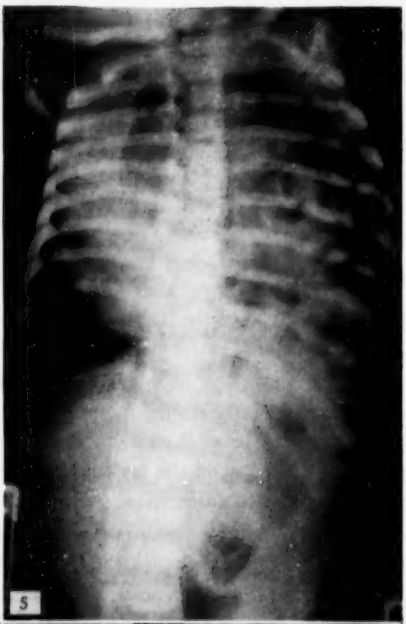
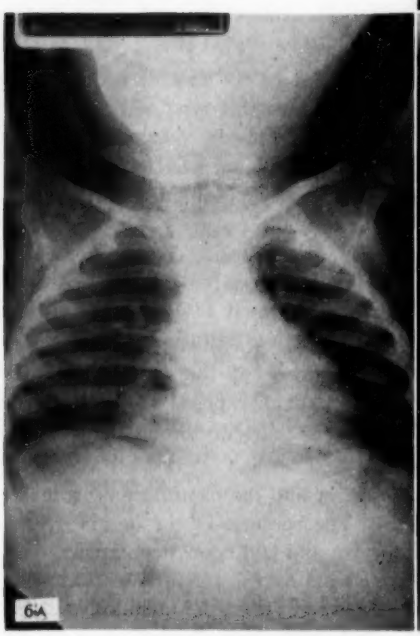
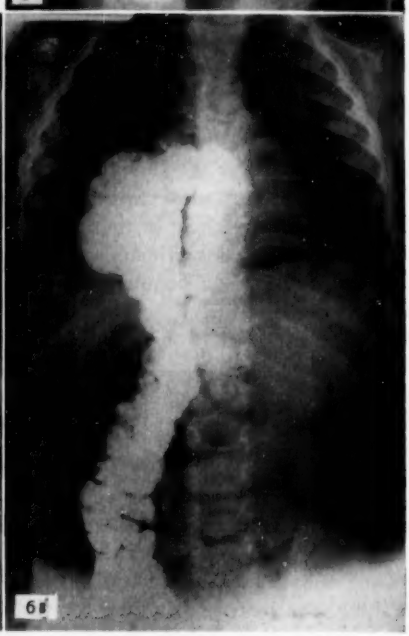


Fig. 5.—Hernia through the left foramen of Bochdalek with marked displacement of the mediastinum toward the right. Only a few air pockets in the descending colon are visible in the abdominal cavity.

Fig. 6.—*A*, x-ray examination of Case 30. Radiolucent area at right cardiophrenic junction suggested lung cyst, duplication, or diaphragmatic hernia. Upper gastrointestinal series with barium was negative. *B*, barium enema showed herniation of the colon into the right chest. This was through the foramen of Bochdalek and had a true hernial sac.





produce obstruction typical of malrotation. This is another factor favoring the abdominal approach. Often the color of the intestines reduced from the hernia is a dusky purple, but upon application of warm, moist laparotomy pads the color promptly returns to normal. In no instance was gangrene of the bowel present, necessitating resection.

Closure of the diaphragmatic defect is the next problem. The opening is often roughly triangular in shape (Fig. 1) and usually 4 cm. in length, with the base of the isosceles triangle 2 cm. wide and located near the upper pole of the kidney. Occasionally, the posterior and lateral portions of the edges of the defect are only a small shelf, or completely absent, so that the anterior edge of the diaphragm must be

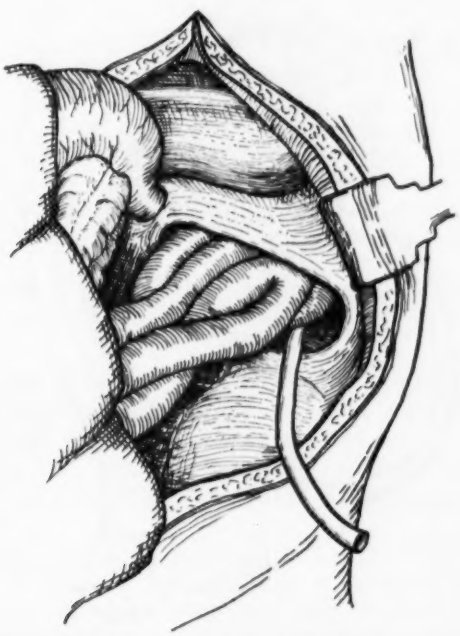


Fig. 7.—Hernia through the left foramen of Bochdalek, showing small intestines being withdrawn from the pleural cavity while air is admitted through the catheter on the right.

brought over and fixed to the posterior and lateral chest wall near the region of the upper pole of the kidney. Freshening of the edges of the defect before repair has long been advocated; however, many have been closed without doing this and the results have been uniformly satisfactory. Imbrication of the edges has also been advised. In many cases this is impossible, and adequate closure can be obtained by coaptation with a series of 3-0 silk interrupted mattress or single stitches placed fairly close together. Before tying the last medial sutures, gentle suction is applied to the catheter in the pleural cavity and gentle inflation of the lungs is attempted by the anesthetist. The catheter is then withdrawn as the sutures are tied (Fig. 8).

Closure of the abdomen often presents a problem. Manual stretching of the abdominal wall may be helpful. If tension is too great and one fears respiratory embarrassment or disruption of the diaphragmatic repair, the skin alone may be

closed. Extensive detachment of the rectus muscles and fascia from the skin to form looser flaps may defeat the purpose of the procedure, since we wish the medial edges of the rectus muscles to be held toward the midline as the abdominal cavity enlarges. After a week or 10 days a secondary closure of the peritoneum and fascia should be performed.

After closure of the wound, it is wise to insert a needle with a 50 cc. syringe attached into the pleural space to be sure there is negative pressure and be able to withdraw air if necessary.

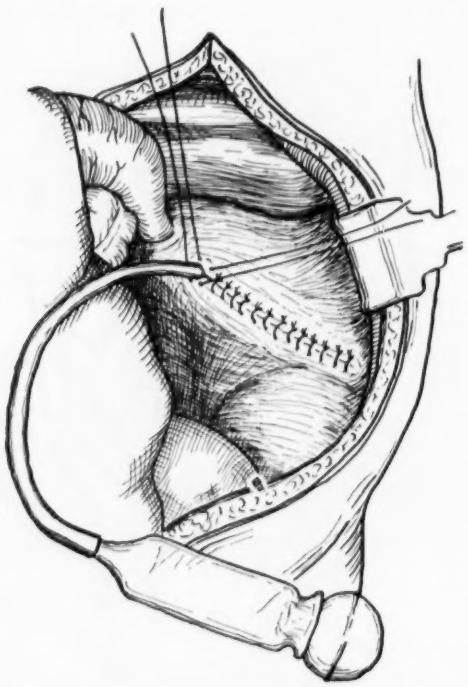


Fig. 8.—Closure of the diaphragmatic defect with interrupted silk sutures. Suction is being applied to the catheter as the anesthetist inflates the lungs. While the last sutures are being tied, the catheter will be withdrawn. The intestines are lying outside the abdominal cavity on the left covered with moist laparotomy pads to facilitate exposure.

Postoperative Treatment.—These patients are placed in an incubator with oxygen or in an oxygen tent, depending on their size. Increase in humidity will facilitate recovery from any trauma of endotracheal anesthesia and will also make secretions easier to raise. Frequent aspiration of the pharynx and change of position of the child from side to side may be required.

Continuous gastric aspiration with a Levin tube may be maintained for 24 to 48 hours, and intravenous feedings are continued until intestinal peristalsis is audible or flatus is expelled.

In the older patients when the thoracic approach is chosen, the incision is made through the seventh interspace posterolaterally. With the patient in reverse Trendel-

enburg position, the bowels usually return easily to the abdominal cavity. We have not found it necessary to crush the phrenic nerve. Healing will be satisfactory without the potentially incapacitating effect of this procedure in a young child.

Since a true hernial sac is often found in the older patient, a majority of the sac may be removed, utilizing the remaining rim of tissue to aid in closing the defect by imbrication of the edges with interrupted silk stitches.

Results.—Twenty-three patients operated upon have had herniation through the foramen of Bochdalek. Only four of these had true hernial sacs, all patients of 6 months of age or older. Four operative deaths have occurred in the group. Each of these cases emphasizes an important point in the treatment of this condition.

Case 2.—R. R. was brought to the Children's Memorial Hospital in the evening, 11 hours after birth, because of cyanosis and dyspnea. Diagnosis of a left diaphragmatic hernia was established, but the examiner believed that the child's condition was stable in oxygen and that operation could be postponed until morning. Early the following morning the patient suddenly became increasingly cyanotic, the condition rapidly progressing to complete apnea and circulatory collapse. The infant was rushed to the operating room, an endotracheal tube was inserted and artificial respiration started. In order to increase pulmonary capacity, a rapid laparotomy was done and the intestines removed from the chest. A feeble but audible heart beat resumed, though the patient remained in shock. Rapid closure of the diaphragmatic defect and abdominal wound was accomplished. No bleeding occurred during the procedure owing to the patient's vascular collapse.

Immediately after operation the patient's condition improved, but 12 hours later the patient suddenly died. Postmortem examination revealed a massive left hemothorax and hemoperitoneum.

This forcibly emphasized the urgency of immediate operation in these cases in spite of the apparently static condition. Had the infant been operated upon while in fairly good condition, the bleeding points could have been recognized and dealt with and the child probably would have survived. This possibility of postoperative hemothorax might also argue against the practice of "freshening" the edges of the diaphragmatic defect.

Case 9.—B. B. entered Children's Memorial Hospital at 3 days of age, having had cyanosis and dyspnea since shortly after birth. The diaphragmatic hernia was immediately repaired, and suction was applied to the catheter in the pleural space as the last sutures were tied. At completion of operation the infant's condition seemed good, but, immediately after return to the incubator, cyanosis developed and the heart beat became slow and feeble. In spite of the administration of oxygen, artificial respiration, and stimulants, the patient promptly died. Although autopsy examination was refused, it was decided that the death had been due to persistent left pneumothorax with atelectasis of the right lung, since examination immediately before death revealed no breath sounds over the left chest and only faint breath sounds on the right with a shift of the heart to the right.

It was this unfortunate occurrence that has prompted routine thoracentesis on the operating table immediately postoperatively to determine the degree of negative pressure and aspirate air if necessary.

Case 4.—B. G. entered the hospital 24 hours after birth with the history of cyanosis and mild dyspnea since birth. A diagosis of right diaphragmatic hernia was made, and repair was accomplished through a right thoracotomy. One-half hour after return from surgery the patient's condition was fair, but she had not begun to react and there was a moderate amount of mucus in the throat. Within the next few minutes, the patient suddenly died. Autopsy examination revealed a large mucus plug in the main bronchi.

This emphasizes an important point. In the immediate postoperative period with these infants it is essential to rid the upper respiratory tract of mucus that may be present in excessive amounts due to irritation of anesthetic and endotracheal tube or manipulation of the lungs. Constant attendance and catheter aspiration of the pharynx is necessary. Even more important are the child's own efforts to clear the tracheobronchial tree. Shock or deep anesthesia will prevent this. The anesthetist usually aims to discontinue anesthetic agents long enough before completion of the operation to have the child moving and even crying while the bandage is being applied. After return to the ward, further encouragement of drainage may be obtained by stimulation of crying by slapping the feet, stimulation of cough by pharyngeal aspirations, and frequent changes in position. The principles are the same with all age groups, but it takes a relatively tiny bit of mucus to plug the tracheobronchial tree of a newborn child.

CASE 13.—R. M. was 4 days old when he entered the hospital with the history of dyspnea. The diagnosis of left diaphragmatic hernia was made, and repair was performed via an abdominal approach. The operation was uneventful until closure of the abdominal wound when the anesthetist suddenly lost the pulse beat. Rapid thoracotomy revealed that the heart was almost at a standstill. Massage gave only temporary success, and the child died. Autopsy revealed no pathological cause for death. Since anoxia and hypercarbia were not present and since vagal reflexes did not enter the picture, the anesthetist believes the death was due to excessive deepening of the anesthesia in an attempt to facilitate closure of the abdomen.

Learning from one's own misfortunes is a better but indelible method. Profiting from someone else's mistakes is a much more desirable method but often less emphatic and less durable.

One other case is interesting enough to mention in moderate detail.

CASE 21.—J. A. entered the hospital at the age of 2½ months. She was cyanotic at birth but had improved. The main problem on admission was severe attacks of vomiting. Cardiac examination revealed dextrocardia and a loud systolic murmur over the entire precordium. Roentgenological examination demonstrated that the stomach was in the left chest and that large and small intestines lay in both chests (Fig. 9).

First Operation.—The abdomen was entered through a long transverse incision. The colon, appendix, and some of the small intestine were removed from the chest. The stomach, duodenum, and pancreas were also withdrawn with some difficulty. The defect in the diaphragm lay posterior to the heart and anterior to the spine, extending laterally on both sides with the esophagus hanging free in the center. There was a thin sac keeping the abdominal contents from entering the free pleural cavities. The stomach, duodenum, pancreas, and remainder of the intestines down to the rectum hung on a common mesentery. The right and left lobes of the liver were equal in size and the spleen was absent.

The sac was brought down and utilized in closure of the defect by imbrication. No significant bands or adhesions were found. The patient tolerated the procedure well.

The following four days the child did well but then began to vomit. The vomiting persisted but was never bile-stained. Stomach fluoroscopy revealed that no barium left the stomach at the end of three hours. The child lost weight steadily.

Second Operation.—On the 11th postoperative day the abdomen was explored for the possibility of mechanical obstruction of the duodenum. The stomach lay on the right side with the duodenum acutely angulated and folded beneath it. A large catheter could be passed readily from the stomach through the duodenum and well into the jejunum, ruling out an intrinsic web stenosis. The duodenum was straightened and fixed loosely to the left parietal abdominal wall. The child did not improve after the second operation. Stomach fluoroscopy five days later still revealed no passage of radiopaque material beyond the stomach. The patient's condition deteriorated.

Third Operation.—Six days after the second operation, another laparotomy was performed with the use of local anesthesia, and, though no mechanical obstruction could be found, a gastroenterostomy was performed in the hope that vagal injury might be the basis for poor stomach emptying.

After gastroenterostomy the child slowly recovered, with retention of oral feedings and gradual weight gain. Before discharge, one month after the third operation, the cardiac status was reevaluated. X-ray examination showed dextrocardia, enlargement of the heart, and increased vascularity of the lungs. A diagnosis of intraventricular septal defect was made.

Fig. 9.—X-ray examination of Case 21. Barium studies show the stomach and intestines herniate through a midline defect into both pleural cavities. Note dextrocardia and symmetrical liver shadows.

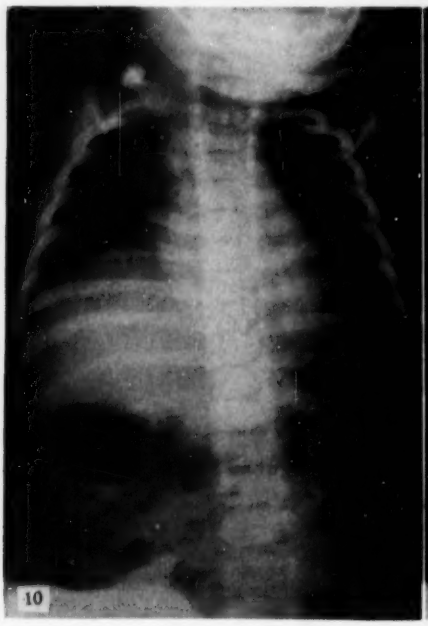
Fluoroscopy revealed no recurrence of the diaphragmatic hernia. Several months after returning to her home in South America, the child died in heart failure. Autopsy was reported to confirm the diagnosis of intraventricular septal defect.

EVENTRATION OF THE DIAPHRAGM

Eventration of the diaphragm seems to be a general stretching out of the diaphragm with an apparent relative diminution of the muscular elements about the periphery. The etiology may be a failure of the muscular migration between the

layers of pleura and peritoneum making up the diaphragm. If musculature were poorly formed, the increase in abdominal contents pushing upward and the development of normal intrathoracic negative pressure might result in a stretching out of the membranous diaphragm until it rises well into the chest.

At one time, we entertained the possibility that absence or nonfunction of the phrenic nerve on the affected side might be the cause of this deformity. Several newborn patients have been treated at Children's Memorial Hospital for paralysis of the right diaphragm due to birth injury of the phrenic nerve. Dyspnea and cyanosis necessitated oxygen therapy. X-ray pictures of the chest revealed a situation almost identical to that seen in eventration (Fig. 10). Fluoroscopic examina-



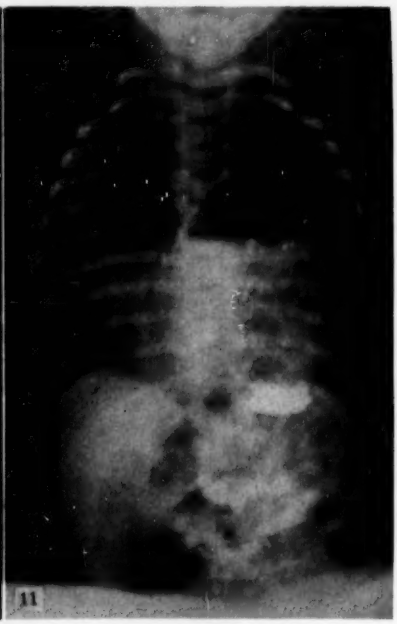


Fig. 10.—X-ray examination in a case of paralysis of the right diaphragm due to birth injury of the phrenic nerve. Note that the dome of the diaphragm bulges halfway up toward the apex of the right chest, simulating eventration of the diaphragm.

Fig. 11.—X-ray examination of the chest in Case 20 shows displacement of the mediastinum to the right. The smooth rounded line above the air-fluid levels on the left represents the thinned-out diaphragm typical of eventration.

tion of two patients after repair of eventration revealed synchronous movements of the two sides of the diaphragm, disproving this theory.

Diagnosis.—Usually symptoms from this condition are absent or minimal. Of four patients we have observed, only one had mild symptoms of some dyspnea just after feeding. In the other three cases routine chest films had disclosed the deformity.

X-ray examination is essential for the diagnosis. Anteroposterior and lateral views will show air-filled bowel in the lower thoracic area well above its normal level. Solid structures, such as liver and spleen, may give the impression of a tumor

in the lower chest cavity. Instead of bowel being present above a portion of normally placed diaphragm, there will appear to be a general elevation of the diaphragm extending from the periphery, and a definite line can be made out representing the diaphragm (Fig. 11). Pneumoperitoneum has been advocated to delineate the diaphragm more accurately.

Operation.—Treatment need only be urged in those cases that have definite symptoms referable to the deformity. Figure 11 illustrates such a patient with a rather marked deformity causing some shift of the mediastinum and moderate symptoms. Operation consists of a transthoracic approach with excision of a major portion of the fibrous dome of the diaphragm, leaving a few centimeters edge adjoining the muscular portion for imbrication with interrupted silk sutures.

With the return of the diaphragm to its normal level, the symptoms are alleviated and there seems to be no tendency for the repaired leaf to stretch out again.

CONGENITAL ABSENCE OF THE DIAPHRAGM

We have been fortunate in never having encountered complete absence of one entire side of the diaphragm. From the descriptions and illustrations of this defect in most of the literature, this term would appear to be a misnomer, since a sizable portion of the anterior half of the diaphragm usually is depicted as being present. The condition seems to be merely a matter of the degree of failure of closure of the posterior portion of the diaphragm.

As mentioned above, the posterior defects in the diaphragm occasionally present no shelf of tissue whatever along the posterior and lateral chest wall and repair poses a difficult problem. We have always been able to pull the anterior portion of the diaphragm backward enough to stitch its edge to the intercostal muscles and periosteum of the lower ribs. If larger defects are encountered, various methods of closure have been suggested, such as partial thoracoplasty to bring the posterior and lateral lower chest wall over to the remaining anterior portion of diaphragm or utilization of portions of the anterior abdominal wall as a muscular flap to bridge the gap.

COMMENT

It will be noted that 15 of the patients were less than 6 days of age at the time of surgical repair. All but one had herniation through the foramen of Bochdalek without any confining sac. This resulted in severe and progressive dyspnea and cyanosis requiring immediate surgical treatment. Abdominal operative approach was used in all but one patient. All four deaths attributable to the hernia and its repair occurred in patients in this age group. As has been mentioned, these deaths might have been averted by alteration in anesthesia technique and in general pre and postoperative care.

Another distinct group appears in the six patients coming for initial treatment after the age of one year. These children presented mild symptoms or none at all. Each had a congenital defect of the diaphragm with a confining sac which limited the degree of herniation of the abdominal viscera into the thoracic cavity. One child with an eventration of the left diaphragm was not operated upon since the deformity was minimal and symptoms were absent. The rest underwent operative repair via a transthoracic approach.

Between these two extremes there were 12 infants from 1 week to 1 year of age with a variety of congenital diaphragmatic defects and with varying degrees of symptoms. It might be concluded that if a patient develops symptoms attributable to a diaphragmatic hernia before one year of age, prompt surgical repair must be advised, and if the symptoms begin less than a week after birth, it must be considered an extreme emergency. However, if mild symptoms bring attention to the hernia after a year of age, we might presume that there is a self-limiting process and that surgical treatment can become an elective procedure decided on the merits of the individual case.

Aside from the four operative deaths and the two patients that later died of other congenital anomalies, all of the patients have done well. The diaphragmatic repairs have been successful, except for one patient with an esophageal hiatus hernia (Case 22) who developed a slight recurrence that has required no further treatment.

SUMMARY

Thirty-three patients with various types of congenital diaphragmatic hernias are discussed, highlighting some of the problems related to each type of hernia.

In patients under a year of age, especially under 1 week of age, symptoms are usually severe, there is usually no confining hernial sac, and emergency operative repair is necessary.

If the hernia is discovered after one year of life, the symptoms are mild or absent, there is a confining sac of some type, and surgical repair may be considered at leisure.

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DISCUSSION

Dr. Earle B. Kay, Cleveland: I should like to discuss Dr. Riker's paper, particularly with reference to the group under 6 years of age, and to stress the advantages of the thoracic rather than the abdominal approach, for the following reasons:

These small children, and particularly the newborn babies, are acute emergencies because of lack of sufficient functioning pulmonary tissue. The hemithorax on the affected side is filled with herniated abdominal content. The lung on this side usually has failed to aerate. The mediastinum is shifted to the opposite side, causing compression of the contralateral lung. Usually, only the base of this lung is aerating. Such infants are cyanotic, dyspneic, and appear desperately ill. Time is an important factor. The speed of the thoracic approach allows the hernial contents to protrude through the incision, the lung to expand, and the mediastinum to return to its anatomical position, all of which cannot be accomplished with the same rapidity and sureness through an abdominal approach.

Cardiac arrest is a frequent complication during the operative procedure. This can be dealt with more effectively under the direct vision and adequate exposure of a thoracic approach.

Postoperative pulmonary complications, as shown by Dr. Riker, are a frequent cause of death. By means of the thoracic exposure it is possible to know at the time that the lung is expanded and that proper thoracotomy drainage is being employed.

Lastly, as was mentioned, it is difficult to get the gastrointestinal content, liver, and spleen into the abdomen and to be able to close the abdominal incision. In several of the cases mentioned, only the skin could be closed. In the infant's development, the abdominal cavity is small, the diaphragm is at a lower level, and the hemithorax is larger than normal. Growth has not allowed any place in the abdominal cavity for the herniated content.

I have found, in the majority of such small infants, that even trying to reduce the hernia through the thoracic approach is difficult. However, if the lateral attachments of the diaphragm are severed from the chest wall for several inches, beginning at the defect in the diaphragm,

which is usually at the pleural peritoneal foramen posterolaterally, the herniated content can be easily replaced into the abdominal cavity. The diaphragm can then be reattached to the chest wall at a higher level by passing mattress sutures through the diaphragm and through the chest wall, and tying them over rubber tubes on the outside. Additional individual sutures can also be employed within. A thoracic approach employing such a technique can avert many of the complications that might otherwise develop.

DR. JOHN M. DORSEY, Evanston, Ill.: First, I should like to compliment Dr. Riker on his results. He has applied very strict criteria in analyzing the deaths, I am sure. Most of the congenital diaphragmatic hernias will probably continue to be cared for in children's hospitals because of the experience of the physicians there and because of the tendency of other physicians who recognize these conditions to send their patients to children's hospitals and to experts when they are available.

However, I think it is important for those of us in other hospitals, who see such hernias, to recognize certain things. Certainly it is an established fact that the urgency of the repair in an infant who is known to have a diaphragmatic hernia is paramount. I should like to call attention to one condition, however, which has been confused with congenital diaphragmatic hernia, and that is, congenital cystic disease, particularly of a basal segment of the lung. In the haste to operate upon a congenital hernia, certainly we should be aware that this disease process may be confused with hernia, causing cyanosis and respiratory difficulty just as will a hernia. Those patients are the ones that should not be operated upon.

In the in-between group are some infants who at birth apparently have hernial defects but in whom herniation has not occurred. I have seen two such infants.

[Slide] This first infant was born at the Presbyterian Hospital in Chicago, and, because of some temperature elevation, it had occasion to have its chest x-rayed. This is the x-ray film of the chest at birth, which is essentially normal except for a little infiltration in the left upper lung field.

[Slide] This is a slide of the child's chest at the age of 4 years. This child went on to develop, when seen later by a pediatrician, a very sizable left foramen of Bochdalek hernia.

[Slide] This is a lateral view of the same chest, showing that a child at birth can have a hernial defect but no hernia.

[Slide] This shows a child that was not operated upon early because of too much study in the preoperative period. That was before we recognized the urgent need for operation. It shows the smallness of the defect, this time in the right diaphragm, which could have been very simply repaired and the hernia taken care of.

[Slide] The next patient is also one with a right diaphragmatic hernia which did not appear until the eighth week of life. Symptoms of cyanosis and respiratory difficulty gave the pediatrician the impression that this child had pneumonia. Instead, her difficulty was that of right diaphragmatic hernia. She had been well until, suddenly, in the eighth week of life, the symptoms appeared, and apparently the herniation occurred at that particular time. She was successfully operated on the day of her admission to the hospital.

DR. HIRAM T. LANGSTON, Riverside, Ill.: Attention has been frequently called to the fact that the difficulty in repairing these diaphragmatic hernias may reside in getting the bowel back into the abdomen. I would like to call your attention to the fact that the reverse and the counterpart of that can occur, and you may have difficulty with the thoracic side of the diaphragmatic hernia.

Recently I had this very forcibly called to my attention. I did not think it could happen. However, if these hernias that occur in patients of very young age are not repaired and no complication occurs so that they become long-standing, the diaphragm apparently will assume the complete inspiratory position. The lung will have been displaced upward and so molded by the hernial mass that you may have trouble getting the two to meet.

I think it is important to realize that, regardless of whether an abdominal or a thoracic approach is used, there may be difficulty in getting the thoracic viscera to reaccommodate themselves if they have been displaced and held in that position long enough.

DR. FRANKLIN E. WALTON, St. Louis: The point I would like to emphasize is the fashion in which this subject concerns general surgeons.

For example, rather recently I was asked to see a five-day-old baby that had just been admitted to St. Louis Children's Hospital with an obvious peritonitis. An open film of the abdomen revealed radiopaque sheets of material which caused both the pediatrician and members of the department of radiology to suspect this might be a case of meconium peritonitis. [Slides] After the fluid balance had been corrected, this child's abdomen was explored through a transverse incision, and the child did have an overwhelming meconium peritonitis—but the pneumoperitoneum and the leak of the meconium throughout the peritoneal cavity came from the gangrenous posterior wall of the stomach which was incarcerated in the left thoracic cavity, through a diaphragmatic hernial defect!

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PHYSIOLOGICAL AND PATHOLOGICAL EFFECTS OF LONG-TERM POLYVINYLPYRROLIDONE RETENTION

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A VARIETY of natural and synthetic colloidal solutions have been used for the reestablishment of the circulation, but experience has emphasized that the ideal fluid for use in hemorrhagic or traumatic shock is blood of an identical grouping. Since methods have not been developed for the stockpiling of blood, it has become readily apparent that a sufficient supply of blood would not be available for emergency use for mass casualties resulting from an atomic attack. The search for a plasma substitute suitable for stockpiling has therefore been intensified in recent years. Polyvinylpyrrolidone, or PVP, is one of the three agents under intensive investigation for this purpose. It is an entirely synthetic product which is water-soluble, hydrophilic, and of high molecular weight. Originally introduced in 1943 by Hecht and Weese,[1] it was administered to approximately one-third million German casualties at the Russian front, and a summary of the results of a million infusions with PVP was published in 1951.[2] The effectiveness of this agent as a plasma volume expander in the treatment of shock has been corroborated by many other investigators.

One of the chief potential limitations of PVP has been the demonstration that 35-49% of it is retained indefinitely in the body after intravenous infusion.* This limitation has stimulated our interest in investigating any undesirable or harmful effects which might be associated with this storage phenomenon. A previous report [4] described the histologic studies of the liver made on patients during a follow-up period of 13 months after the intravenous injection of 1,000 cc. of 3.5% PVP. A second report [5] was on studies of the blood, renal function, hepatic function, and liver biopsies in the same group of patients during a 15-month period of follow-up. The present report consists of serial observations made on the same group of patients over a follow-up period of 20 months. Included are the preliminary studies

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From the Departments of Surgery and Pathology and the Gastric Laboratory of the Department of Internal Medicine, University of Cincinnati. Work done under the auspices of the National Research Council.

* Reference 3, and Fine, J.: Personal communication to the authors.

carried out on seven patients who came to necropsy at intervals of 4 to 19 months after the administration of PVP. In evaluating PVP as a plasma substitute suitable for national defense, it is important to determine whether or not the prolonged retention of PVP produces harmful effects on the physiology and structure of organs and tissues in which it has been deposited.

MATERIAL AND METHODS

It has been possible to obtain clinical and laboratory data on 23 of the 25 patients originally injected with 1,000 cc. of 3.5% PVP intravenously. The data have consisted of serial laboratory studies made every two to eight weeks and have included complete blood count, hemoglobin level, hematocrit reading, urinalysis, blood urea nitrogen content, phenolsulfonphthalein excretion, and sedimentation rate obtained by the Wintrobe procedure. Various liver function tests were also done. These consisted of determination of sulfobromophthalein (Bromsulphalein) retention, cephalin flocculation, zinc sulfate and thymol turbidity, total serum lipids, serum alkaline phosphatase, and serum bilirubin. In addition to the histologic studies on the interval liver biopsy specimens, autopsy studies have been possible on seven patients who have died of intercurrent and unrelated causes.

RESULTS

No anaphylactic effect has been reported in any of the patients during or immediately after the infusion of PVP. Likewise, there have been no toxic effects noted clinically immediately after the infusion or later. Enlargement of the spleen or liver has not been found.

No disturbance in blood grouping was reported in any of these patients.

The last studies done on the blood during the follow-up period of 20 months have continued to show a slight or moderate elevation in the red blood cell count, hemoglobin level, and hematocrit reading. A suitable explanation for these changes has not been determined as yet. The white blood cell count and differential count have not changed appreciably.

The erythrocyte sedimentation rate was found to be elevated in all cases immediately after infusion. Subsequently, within six months, there was a decline in the sedimentation rate in seven of the patients. Of the remaining patients all but two have shown persistent elevation during a period of follow-up of 16 months.

No alteration in liver function was noted as evidenced by the results in thymol turbidity, cephalin flocculation, total lipids, or serum bilirubin tests. There was, however, a temporary elevation in the cephalin flocculation in 11 cases and an abnormal retention of sulfobromophthalein in 5 patients during the first two months.[5] Thereafter, only sporadic elevations were observed.

As previously reported,† biopsy preparations of the liver stained by the hematoxylin and eosin methods failed to show any evidence of histologic alterations during the six to eight week interval. No material was procured for biopsy prior to the second week after infusion. Studies are contemplated for the purpose of corroborating the observations of Hüsselmann and others relative to the early and transitory hygroscopic lesions in parenchymal epithelium. We have not noted these lesions in our specimens obtained at a later period. After the eighth week, deposits

† References 4 and 5.

of pale, basophilic, globular material appeared within the Kupffer cells in increasing amounts. Later specimens revealed larger accumulations of this material, which distended the phagocytes or filled the sinusoids, compressing the adjacent liver cells. In the biopsy specimens obtained between the 6th and 13th month after infusion, 22 of the 23 cases showed evidence of similarly deposited material.[5] In three cases heavy accumulations of the basophilic material were associated with a mild inflammatory reaction consisting of lymphocytes and histiocytes. Occasional fibroblasts were noted in this area, but collagen deposition was not detected. A variety of histochemical methods have failed to prove conclusively the nature of the accumulated material, because of its chemical inertness, but there is little doubt that the substance is PVP.

It has been possible to collect data from seven autopsies performed on patients in this group who died of a variety of causes unrelated to the PVP administration.

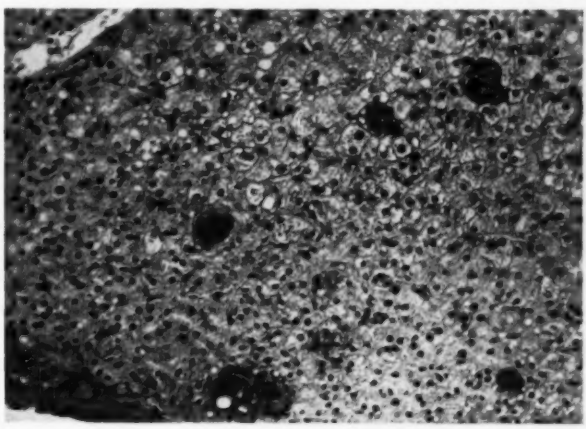

Fig. 1.—Deposits of PVP in needle liver biopsy specimen. Rounded black masses are collections of foreign material distending sinusoids. Hematoxylin and eosin; × 160.

Two of these patients died four and six months, respectively, after infusion. The remaining five succumbed at intervals of 13 to 19 months.

Using a special method of differential staining devised to highlight PVP by means of its avidity for Congo red [6] and counterstaining the section with light green,‡ we made a search to determine the distribution of the material in the various tissues of the body.

PVP was retained in significant amounts in each patient. It was regularly demonstrable in the spleen, lymph nodes, liver, bone marrow, and adrenal cortex (Figs. 1 and 2). In these regions the deposits appeared in histiocytes, which were uniformly filled with the substance. Aggregations exceeding the capacity of histiocytes lay free in the interstitial tissues, where no significant evidence of reactive inflammation or fibrosis was detected. Another common site was the interglandular stroma of the gastric and intestinal mucosa. Lying within histiocytes, this phenomenon probably reflected the course of excretion of these cells into the lumen of the alimentary tract.

‡ Gall, E. A., and Freiman, D.: Unpublished data.

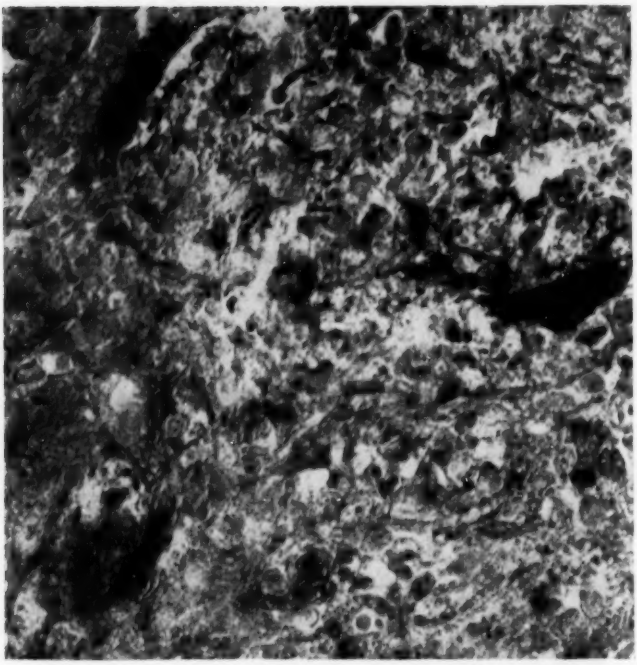

Fig. 2.—Deposits of PVP in section of spleen secured at necropsy. Irregular black masses are deposits of the material, largely within histiocytes. PVP stains brilliant red with Congo red, while background is stained green. Congo red-light green stain; × 650.

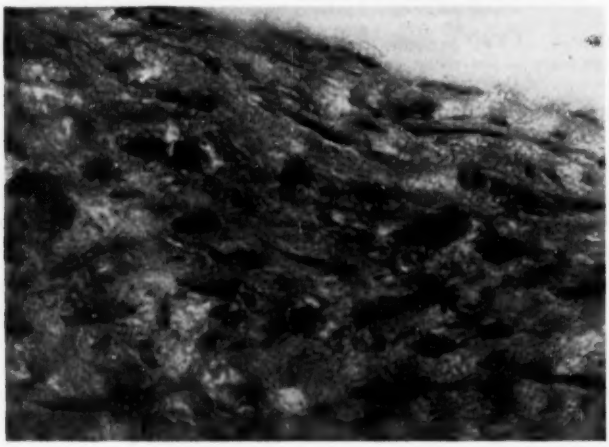

Fig. 3.—Arteriosclerotic plaque in aorta containing PVP deposit. Grayish-black masses with irregular shape consist of foreign material stained with Congo red. Congo red-light green stain; × 650.

Of particular interest was the inconstant demonstration of the polymer in the heart, lung, arteriosclerotic plaques of the aorta, pancreas, kidney, bladder, prostate, gall bladder, esophagus and thyroid (Fig. 3). None was found in sections of the ovary, testis, pituitary, brain, spinal cord, peripheral nerve, or skeletal muscle. Several examples of metastatic carcinoma also were free of deposit.

The inconstant appearance of PVP in these nonstorage organs is thought to represent a response to local injury, inflammation, or repair. It would appear that the mobile phagocytic elements of the body, though laden with PVP, are not restricted in relation to chemotaxis or motility. They appear, therefore, in their usual manner in exudative lesions, where their presence is highlighted by their stainable content. With the data at hand it is not possible to determine whether the phagocytic or immunogenic properties of the affected histiocytes are impaired. This question is to serve as the basis for additional investigation.

ANALYSIS

These studies indicate that retention and storage of PVP persist for at least 20 months after intravenous infusion of only 1,000 cc. of 3.5% solution. Although many investigators have not found pathological changes in the viscera of animals or human patients after intravenous infusions of PVP, others, such as Hüsselmann,§ Schallock,[7] Ammon and Müller,[8] and Grönwall,[9] have described lesions similar to those found by us.

The value of colloidal solutions as plasma substitutes rests primarily on their immediate therapeutic action and any untoward effects which may be associated with their use. Presumably because of its inert chemical nature, no overt clinical reactions either toxic or allergic were noted.

Preinfusion erythrocyte sedimentation rates were not obtained in our studies. The high index of elevation following infusion makes this variation significant, but it is probably not important from a practical or clinical standpoint. It is interesting to note that similar elevations of the sedimentation rate were described for periods up to three weeks after infusions of PVP by Thorsen and Hint in 1950[10] and by Haller, Clift, Jameson, and Swinton in 1953.[11] The persistence of the elevated sedimentation rate in our cases has not been described previously, and it suggests that some PVP remains in the circulation for long periods of time, up to 15-20 months. This possibility should be investigated further.

The prolonged retention of PVP by the body is unquestionably a disadvantage which must be considered carefully. Since this colloidal substance is not metabolized or broken down into components small enough to permit excretion, storage occurs for periods of at least 20 months after relatively small injections, of 1,000 cc. The storage develops in the various organs, particularly in those comprising the so-called reticuloendothelial system.

It is generally considered inadvisable to administer in any quantity medicaments which are stored permanently in important organs or tissues. Their possible effect on the function of those structures or the production of an inflammatory or foreign body reaction is to be kept in mind.

To date no significant evidence has been found in our data which indicates that an amount of 1,000 cc. of PVP appreciably effects the function of the liver, kidneys,

§ Gall, E. A., and Freiman, D.: Unpublished data.

or bone marrow. There is suggestive evidence, however, that slight and transitory impairment of hepatic function occurred in some cases. With considerably larger doses of PVP it is conceivable that serious physiological alterations might occur, but this has not been proved.

Minor inflammatory reactions presumed to be related to PVP have been observed in only three of our cases, but it is noteworthy that the amount of PVP deposited in the liver and other tissues has slowly and progressively increased throughout the study. The findings necessitate continued study of these cases to determine whether or not the retained PVP ultimately causes significant physiological and pathological alterations or whether it is ultimately excreted. If it is shown to cause such alterations, it will be necessary to abandon its use, as was the case with other substances previously used for this purpose, such as acacia (gum arabic) and pectin.

SUMMARY

Further studies were conducted on 23 patients who had received an intravenous infusion of 1,000 cc. of polyvinylpyrrolidone (PVP) 20 months previously. These studies indicate that PVP was stored in the body in every case and persisted without signs of diminishing up to 20 months. The various physiological and pathological alterations which were found in this group have been summarized. The investigations will be continued and intensified to determine whether the prolonged retention of this material ultimately causes sufficient deleterious effects to preclude its use as a substitute for plasma.

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TOLERANCE OF ELDERLY SURGICAL PATIENTS TO INTRAVENOUS DEXTROSE AND WATER SOLUTIONS

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IT HAS been well substantiated that the proportion of aged in the population of the United States is increasing. In 1900, the average life expectancy was 48 years. By 1950, it had increased to 68.27 years. During the period 1930-1940, there was a 7% increase in the total population of this country, but during the same period the number of persons between the ages of 65 and 74 had increased 35% and the number over 75 years by 38%.[1] As a natural consequence, there has been an increase in the number of patients undergoing surgery in the latter decades of life. At the University of Michigan Hospital there has been a 112% increase in the num-

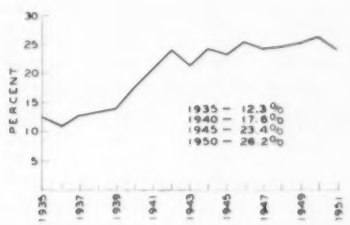

Fig. 1.—Per cent of total operations in patients aged 60 years and over, University of Michigan Hospital, 1935 to 1950 (Collier, F. A., and Dobbie, R. W.: Unpublished data).

ber of major abdominal operations in patients more than 50 years of age in 1950, as compared with the number in 1940. Furthermore, a steady increase in the relative number of patients over 60 years of age undergoing major surgery has been observed. This proportion has risen from 12.3% in 1935 to 26.2% in 1950 * (Fig. 1).

Little doubt remains that such surgery not only saves lives but also may contribute importantly to better health and greater enjoyment of the twilight years. Analysis of operative mortality rates and observations of the postoperative course of elderly patients has provided two facts: (1) Patients in this age group are able to tolerate elective surgical procedures of considerable magnitude surprisingly well, provided that their general physical condition is reasonably good and careful preoperative, operative, and postoperative care is scrupulously observed, and (2) emergency procedures are not so well tolerated as in younger persons.[2]

From the Department of Surgery, University of Michigan Medical School.
Read at the 11th Annual Meeting of the Central Surgical Association, Detroit, Feb. 19, 1954.
* Coller, F. A., and Dobbie, R. W.: Unpublished data.

Objective knowledge of the response of elderly patients to stress of injury and operation, however, is meager. The use of parenteral fluids during surgical care of these patients has too often been an empirical modification of accepted procedure used in younger patients. As a result, the use of such parenteral fluids has probably been instituted with less rational background in these elderly patients than in any other age group because we lack knowledge of the chemical anatomy of water and electrolyte physiology, as well as accurate knowledge of physiology and pathological physiology, in the senescent patient. This study was initiated with the objective of learning more about the response of aged patients to stress imposed by surgery.

METHODS

Patients of more than 70 years of age, reasonably well preserved and undergoing elective operation, were selected for this study. The hazards of using chronological age as an index of physiological age are well recognized. Some standard, however, should be used. It is felt that if the investigated group can subsequently be made large enough this factor will tend to equilibriate itself.

The cardiovascular status was considered to be satisfactory if the systolic blood pressure was less than 170 mm. Hg, the physical examination revealed no evidence of cardiac decompensation,

TABLE 1.—*Preoperative Renal Function Studies*

Patient	Age, Yr.	NPN, Mg./100 Cc.	Maximum Observed Concentration	Urea Clearance (Normal 75%)	Creatinine Clearance (Normal 100 Liters/24 Hr.)
A. L.	74	23	1.024	40	130
J. G.	73	23	1.016	90	36
J. S.	87	22	1.020	30	100
L. S.	72	33	1.025	146	100
I. P.	71	31	1.030	56	76
C. S.	79	31	1.018	62	71
I. S.	87	39	1.024	53	90
E. M.	71	43	1.023	36	114
M. S.	76	23	1.020	94	...
P. S.	71	42	1.025	..	...

and there was no history of cardiac decompensation, severe coronary occlusion, or angina pectoris. Electrocardiograph evidence of chronic myocardial disease was not considered a contraindication for inclusion in the study group.

Preoperative renal function studies included the following: routine examination of the urine, an 18-hour maximum urine concentration test, and blood nonprotein nitrogen, urea, and creatinine clearance tests. Patients showing gross abnormalities upon routine examination of the urine were not considered suitable subjects for this study (Table 1).

Preloading with water or electrolyte was not attempted. Patients were kept on a standard hospital diet during preoperative work-up, with the exception of those who gave a history of weight loss or had obviously lost weight during their illness. Supplementary feedings, consisting of high-caloric, high-protein feedings, were strongly encouraged in this group. Hemoglobin levels below 12 gm. per 100 cc. were restored by whole blood transfusions.[3]

Fluids administered during operation were limited to the replacement of estimated blood loss and/or dextrose in water solutions given at a rate not to exceed 500 cc. an hour. No more than 2,000 cc. of dextrose solution was given to any patient during the 24 hours following operation. Fluid maintenance after the day of operation was provided by varying amounts and concentrations of dextrose in water with selective, additive small amounts of Ringer's solution in certain cases. Continuous infusion was utilized. Primary emphasis in this study has been placed upon tolerance of such fluids administered intravenously. Certain observations as regards electrolyte metabolism have been included in selected cases, however. Data obtained from a limited number of pre and postoperative determinations of blood [4] and extracellular fluid [5] volume studies are shown in Table 13.

Detailed electrolyte studies were done in selected patients, including determinations of serum electrolyte levels before operation and during and at the end of the study period. Postoperative urinary electrolyte excretion studies were done in two patients.

Serum and urine sodium and potassium were determined by the Perkin-Elmer flame photometer and serum and urine chloride by the method of Schales and Schales[6]; CO_2-combining-power determinations were done with the Van Slyke volumetric gas apparatus; NPN, by the Folin-Wu technique; BUN, by the Gentzkow technique,[7] and serum proteins, by a modification of the Weichselbaum method.[8]

Measured amounts of ice chips were permitted orally in order to alleviate thirst and to provide greater comfort of the mucous membranes of the mouth and throat. Insensible loss from the skin and lungs as well as preformed water of metabolism are uncalculated variables in this study. Because of the lowered oxidative processes and metabolism, it is likely that both these factors are only one-half to two-thirds those of younger patients.[9]

This study does not include a sufficient number of cases for accurate statistical analysis. It is felt, therefore, that the presentation and discussion of case histories will provide the most satisfactory method of reporting the data.

RESULTS

Preoperative determination of renal function in 10 patients (Table 1) presented considerable variation. In general it may be stated that kidney function in all these patients showed some degree of diminution when compared with that in younger persons. Concentration ability was good but not excellent. Only two were unable to concentrate to 1.020. The highest concentration observed was 1.030 (Patient I. P.), but both urea and creatinine clearance tests were subnormal in this patient. Only three of nine patients had normal or higher than normal urea clearance tests. Four of eight creatinine clearance tests were normal or exceeded normal values. Variations from accepted norms, however, did not reflect inability to excrete large loads of water given several patients in this study. Further experience has suggested that in elderly patients a maximum concentration test has been satisfactory for estimating the ability of the kidney to manage postoperative intravenous water and dextrose solutions.

Case 1.—I. S. (U. H. #752257), 87 years old, was admitted for repair of an inguinal hernia. Physical examination revealed an elderly white man, reasonably well preserved. Weight 120 lb. (54.4 kg.), height 5 ft. 6 in. (168 cm.). Blood pressure 120/80, pulse rate 80, rate and rhythm normal. The remainder of the physical examination was normal except for the presence of a large direct left inguinal hernia.

Laboratory
- Urine
  - Routine specimen negative
  - Max. 18 hr. conc. test 1.024
  - Urea clearance 50% one hr.
    53% two hr.
  - Creatinine clearance 90 L./24 hr.
- Blood
  - Hemoglobin, 12.5 gm./100 cc.
  - W.B.C., 8,100
  - Sodium, 140 mEq.
  - Potassium, 3.9 mEq.
  - Chloride, 101 mEq.
  - CO_2, 55 vol. %
  - NPN, 39 mg./100 cc.
  - Total serum protein 6.8 gm./100 cc.
    - Albumin, 4.5 gm./100 cc.
    - Globulin, 2.3 gm./100 cc.
    - A/G, 1.9
  - Creatinine, 1.0 mg./100 cc.
  - Urea nitrogen, 16.5 mg./100 cc.
  - Fasting sugar, 90 mg./100 cc.
  - Kahn negative
  - Prothrombin, 100%

Blood volume

	Preoperative	15 Hr. Postoperative
Total	4,072	3,818
R.B.C.	1.340	1,234
Serum	2.732	2.585

The inguinal hernia was repaired, using N_2O-O_2-ether anesthesia. Measured intake and output for the nine days following operation are shown in Table 2 and Figure 2. A blood volume determination 15 hours postoperatively was 3,818 cc., as compared with 4,072 cc. before operation (Table 13). Nothing was taken by mouth during the first five postoperative days. Urine output

TABLE 2.—*Postoperative Measured Daily Intake and Output Record of Patient L. S. (#752257), Aged 87, Who Had Left Inguinal Herniorrhaphy*

Postoperative Day	Intake, Cc.		Urine Output, Cc.	
	5% Dextrose	Oral		
Day of Operation	2,000	0	500	
1	3,000	0	2,800	
2	2,000	0	3,600	
3	3,000	0	3,000	
4	3,000	0	3,200	
	13,000		13,100	
5		880		200
6		1,210		400
7		2,020		420
8		2,030		480
		6,140		1,500

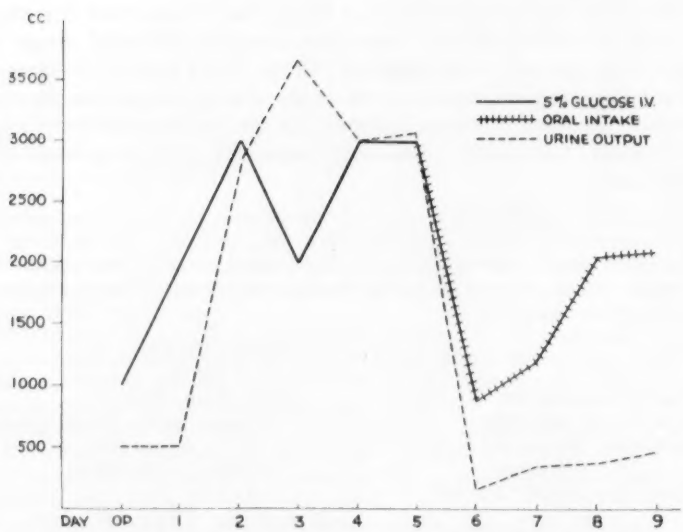

Fig. 2.—Postoperative fluid intake and output record of Patient I. S. (#752257), aged 87, who had left inguinal herniorrhaphy. Observe apparent water loading after resumption of oral fluid. (Reprinted by permission of W. B. Saunders Company; to be published in Surgical Forum Clinical Congress of the American College of Surgeons, W. B. Saunders Company, Philadelphia, 1954.)

during this period was 13,100 cc., with very low specific gravity (1.005 or 1.006). There was good diuresis by the first postoperative day. A measured excess of 100 cc. output over intake would suggest, however, that this patient was in negative water balance even before estimation of insensible loss (Table 2).

Blood chemistries taken at the end of intravenous fluid administration (Table 3) were as follows:

TABLE 3.—*Blood Chemistries Before and After Administration of 13,000 Cc. of 5% Dextrose Solution Intravenously (Patient I. S., #752257, Who Had Left Inguinal Herniorrhaphy)*

	Sodium, mEq.	Potassium, mEq.	Chloride, mEq.	CO_2, Vol. %	NPN, Mg./100 Cc.
Before operation	140	3.9	101	55	30
6th postoperative day	134	8.1	91	47	33

Sodium	134 mEq.
Potassium	8.1 mEq.
Chloride	91 mEq.
CO	47 vol. %
NPN	33 mg./100 cc.

Serum levels of sodium, chloride, CO_2 content, and NPN showed a decrease at the end of the study. The high postinfusion serum potassium level was not observed in other patients and possibly is a laboratory error.

No clinically identifiable deleterious effects were observed during the whole of the study period (Table 3).

Oral fluids were resumed on the sixth postoperative day (Table 2, Fig. 2). There was a sharp drop in urine output and an increase in specific gravity (up to 1.024). During a four-day period of observation on oral fluids this patient was in marked positive water balance, probably representing water loading secondary to the dehydrating effects of large volumes of intravenous fluid.

CASE 2.—J. S. (U. H. #758917), 87 years old, was admitted with a history of a left inguinal hernia of many years' duration.

Physical examination revealed a well-preserved, elderly, white man. Weight 130 lb. (59 kg.), height 5 ft. 7 in. (170 cm.), B.P. 110/80, pulse rate 80, rate and rhythm regular. With the exception of a large left inguinal hernia, the remainder of the physical examination was negative.

Laboratory

Urine

Routine urine negative
Max. 18 hr. conc. test 1.018
Urea clearance 29% 1 hr.
30% 2 hr.
Creatinine clearance 100 L./24 hr.

Blood

Hemoglobin, 14.0 gm./100 cc.
W.B.C., 5,300
NPN, 42 mg./100 cc.
BUN, 11 mg./100 cc.
Creatinine, 1.6 mg./100 cc.
Kahn, Negative
Prothrombin, 100/100 cc.

Left inguinal herniorrhaphy was performed with the use of tetracaine (Pontocaine) hydrochloride spinal anesthesia. Postoperative measured intake and output records are shown in Table 4 and Figure 3. The total intake was 16,570 cc. consisting of 16,000 cc. of 5% dextrose and 570 cc. ice chips. During this same period the urine output was 12,260 cc. The specific gravity averaged 1.005 to 1.006. A measured excess of 4,290 cc. intake over output, without the calculated variables of insensible loss and preformed water of oxidation, would suggest that the dextrose solution did not have the dehydrating effect that it had in the previous patient. No clinical deleterious effects were observed from such large volumes of intravenous fluid. Environmental temperatures were similar for both of these studies.

CASE 3.—E. M. (U. H. #747324), 71 years old, was admitted, giving a 13-year history of abdominal discomfort suggestive of peptic ulcer.

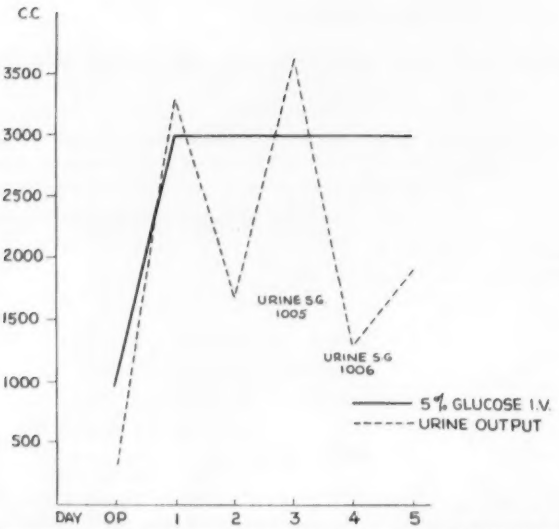

Fig. 3.—Postoperative intake and output record of Patient J. S. (#758918), aged 87, who had left inguinal herniorrhaphy. (Reprinted by permission of the W. B. Saunders Company; to be published in Surgical Forum Clinical Congress of the American College of Surgeons, W. B. Saunders Company, Philadelphia, 1954.)

TABLE 4.—*Postoperative Measured Intake and Output Record of Patient J. S. (#758917), Aged 87, Who Had Left Inguinal Herniorrhaphy*

Postoperative Day	Intake, Cc.		Urine Output, Cc.
	5% Dextrose	Oral Water	
Day of operation	1,000	200	550
1	3,000	370	3,260
2	3,000	...	1,650
3	3,000	...	3,600
4	3,000	...	1,300
5	3,000	...	1,900
Total	16,000	570	12,260
Total intake	16,570 cc.	Total output	12,260 cc.

Physical examination revealed a thin, relatively well-preserved, elderly white man. Weight 100 lb. (45.4 kg.); height, 5 ft. 5 in. (165 cm.); B.P. 125/80; pulse rate 80. No significant physical findings were noted. Upper gastrointestinal x-rays were suggestive of gastric neoplasm in the midportion of the lesser curvature.

Laboratory
- Urine
  - Routine examination negative
  - Max. 18 hr. conc. test 1.023
  - Urea clearance 30% 1 hr.
    36% 2 hr.
  - Creatinine clearance 114 L./24 hr.
- Blood
  - Hemoglobin, 12.0 gm./100 cc.
  - R.B.C., 4,100,000
  - W.B.C., 10,000
  - Kahn, negative
  - Prothrombin, 100%
  - Sodium, 139 mEq.
  - Potassium, 4.5 mEq.
  - Calcium, 9.4 mg./100 cc.
  - Chloride, 103 mEq.
  - CO, 63 vol. %
  - NPN, 43 mg./100 cc.
  - BUN, 29.5 mg./100 cc.
  - Creatinine, 0.9 mg./100 cc.
  - Total proteins, 6.2 gm./100 cc.
    - Albumin, 3.9 gm./100 cc.
    - Globulin, 2.3 gm./100 cc.
    - Ratio, 1.7
  - Blood volume, 4,147 cc. (Table 13)
    - R.B.C., 1,693 cc.
    - Serum, 2,452 cc.
  - Extracellular fluid, vol. 16,600 cc.

At operation a benign gastric ulcer was found, and subtotal gastric resection was done, using intratracheal N_2O-O_2-ether anesthesia. Whole blood, 500 cc., was administered during the operation. Measured intake and output records are shown in Table 5 and Figure 4. Total intake

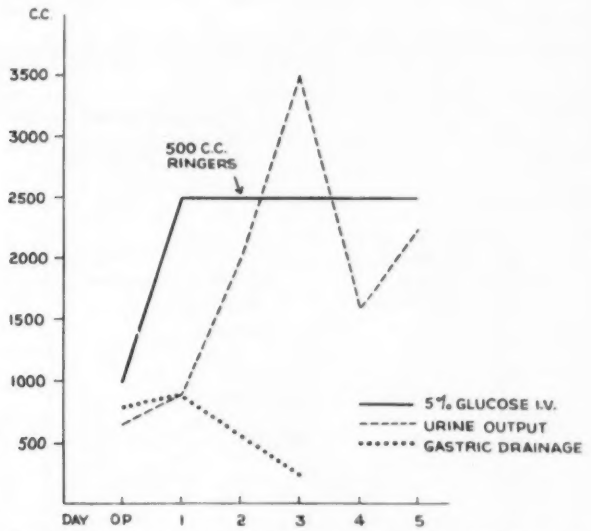

Fig. 4.—Postoperative intake and output record of Patient E. M. (#747324), aged 71, who had gastric resection.

TABLE 5.—*Postoperative Measured Intake and Output Record of Patient E. M. (U. H. #747324), Aged 71, Who Had Gastric Resection*

Postoperative Day	Intake, Cc.			Output, Cc.	
	5% Dextrose	Oral	Ringer's Solution	Urine	Gastric Suction
Day of operation	1,000	...	...	650	800
1	2,500	...	...	900	900
2	2,000	...	500	2,000	250
3	2,500	...	...	3,350	...
4	2,500	...	...	1,600	...
5	2,500	100	...	2,250	...
Totals	13,000	100	500	10,750	1,950
Total intake	13,600 cc.		Total output	12,700 cc.	

TABLE 6.—*Blood Chemistries Before Operation and After Completion of Six Days of Intravenous Dextrose Administration (Patient E. M., #747324, Aged 71, Who Had Gastric Resection)*

	Sodium, mEq.	Potassium, mEq.	Chloride, mEq.	CO_2, Vol. %	NPN, Mg./100 Cc.	Serum Proteins, Gm./100 Cc.	
Before operation	139	4.5	103	63	43	Total	6.2
						Albumin	3.9
						Globulin	2.3
6th postoperative day	132	3.8	92	59	36	Total	6.6
						Albumin	3.7
						Globulin	2.9

during the first six days was 13,600 cc., consisting of 13,000 cc. of 5% dextrose, 500 cc. of Ringer's solution, and 100 cc. of ice chips. During this same period, 10,750 cc. of urine with a low specific gravity (1.006 to 1.007) were excreted and 1,950 cc. of gastric aspirate were removed by suction, the total measured output being 12,700 cc. The measured intake exceeded output by only 900 cc. for the first six postoperative day, with the over-all effect probably being a negative water balance.

Serum electrolyte and protein levels at the end of intravenous fluid administration (Table 6) were as follows:

Sodium, 132 mEq.
Potassium, 3.8 mEq.
Chloride, 92 mEq.
CO_2, 59 vol. %
NPN, 36 mg./100 cc.

Total proteins, 6.6 gm./100 cc.
Albumin, 3.7 gm./100 cc.
Globulin, 2.9 gm./100 cc.
A/G ratio, 1.3

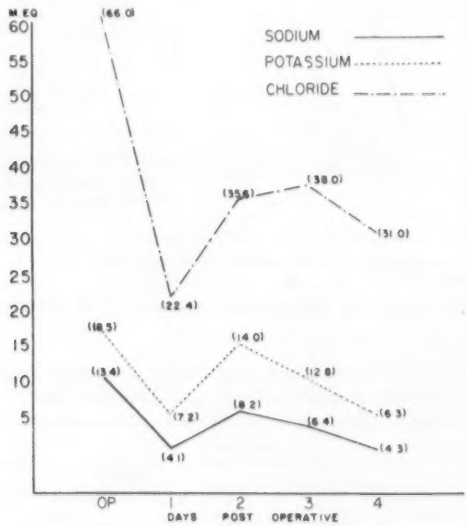

Fig. 5.—Chart showing postoperative urinary excretion of sodium, potassium, and chloride in Patient E. M. (#747324), aged 71, who had gastric resection.

TABLE 7.—*Postoperative Urinary Excretion of Sodium, Potassium, and Chloride (Patient E. M., U. H. #747324, Aged 71, Who Had Gastric Resection)*

Postoperative Day	Sodium, mEq.	Potassium, mEq.	Chloride, mEq.	Comment
Day of operation	13.4	18.5	66.0	
1	4.1	7.2	22.4	
2	8.2	17.0	35.6	500 cc. Ringer's solution intravenously
3	6.4	12.8	38.0	
4	4.3	6.3	31.0	

Although there was some decrease in serum concentration of sodium, potassium, and chloride, no significant clinical symptoms referable to such hypo-osmolarity were observed.

Urinary electrolyte excretion during the first five postoperative days is shown in Table 7 and Figure 5. Renal conservation of sodium was excellent for the whole of the period, although there was a slight increase in urine sodium after the administration of 500 cc. of Ringer's solution.

Relatively small amounts of potassium were excreted despite an apparent negative water balance. In spite of the loss of body electrolyte in the urine and by gastric aspirate, no clinically identifiable deleterious effects of such loss were observed.

Two patients were given only 1,000 cc. of 5% dextrose daily after operation, with small amounts of ice chips orally.

CASE 4.—L. S. (U. H. #761453), 72 years old, was admitted with a six-month history of anorexia, weakness, weight loss, and postprandial epigastric discomfort.

Physical examination revealed a pale, chronically ill, but relatively well-preserved, elderly white woman. Weight 164 lb. (74.4 kg.), height 5 ft. 7½ in. (171 cm.), B.P. 122/52, pulse rate 70, rate and rhythm regular. The remainder of the physical examination was essentially

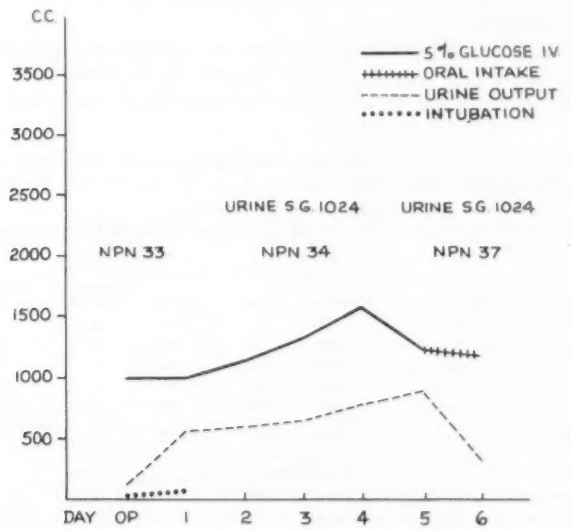

Fig. 6.—Postoperative intake and output record of Patient L. S., (#761453), aged 71, who had gastric resection. One thousand cubic centimeters of 5% dextrose was given daily. Solid black line represents both intravenous and oral intake. (Reprinted by permission of W. B. Saunders Company; to be published in Surgical Forum Clinical Congress of the American College of Surgeons, W. B. Saunders Company, Philadelphia, 1954.)

negative, except for a firm, nonfixed, nontender mass in the epigastrium. Upper gastrointestinal x-rays demonstrated an intrinsic neoplasm of the stomach involving a large portion of the greater curvature.

Laboratory
- Urine
  - Catheterized specimen negative
  - Max. conc. 18 hr. tests 1.026
  - Urea clearance 146% 1 hr.
    60% 2 hr.
  - Creatinine clearance 100 L./24 hr.
- Blood
  - Hemoglobin, 5.4 gm./100 cc.
  - R.B.C., 2,500,000
  - Hematocrit, 20%
  - Sedimentation rate, 14 mm./hr.
  - W.B.C., 7,000 with normal differential count
  - Prothrombin, 54%
  - Kahn, negative
  - Fasting sugar, 81 mg./100 cc.
  - NPN, 33 mg./100 cc.
  - BUN, 17 mg./100 cc.
  - Creatinine, 1.0 mg./100 cc.
- Gastric analysis
  - No free or combined acid
- Stools
  - Negative for blood

Preoperatively this patient was given a transfusion of 2,500 cc. of whole blood. With the use of intratracheal N_2O-O_2-ether anesthesia, a subtotal gastric resection was performed and a large gastric neoplasm removed. Whole blood, 2,000 cc., was transfused during the operation. Subsequent pathological report revealed an undifferentiated adenocarcinoma with extension through the wall and lymph node metastases.

Measured intake and output records are shown in Table 8 and Figure 6. The difference between intake and output was 3,290 cc. Urine specific gravities during this period, however, were high (1.024 or 1.025), and there was a small but gradual increase in the blood NPN, from 33 to 37 mg. per 100 cc. High urine specific gravity and gradually rising NPN would suggest that under the conditions of this study the amount of water administered was inadequate for essential metabolic needs.

Case 5.—A. L. (U. H. #740515), 74 years old, was admitted with symptoms of prostatism of several months' duration.

Physical examination revealed an elderly white man who was thin and appeared chronically ill. Weight 124 lb. (56 kg.), height 5 ft. 7¼ in. (171 cm.), B. P. 120/70, pulse rate 86, rate and rhythm regular. The prostate was enlarged (2+) and firm in consistency. Generalized

Table 8.—*Postoperative Measured Daily Intake and Output Record Correlated with Urine Specific Gravity and Blood NPN (Patient L. S., U. H. #761453, Aged 52, Who Had Gastric Resection)*

	Intake, Cc.		Output, Cc.			
Postoperative Day	5% Dextrose	Oral	Urine	Gastric Suction	Urine S. G.	Blood NPN, Mg./ 100 Cc.
Day of operation	1,000	..	150	30	.....	33
1	1,000	20	530	50	1.024	..
2	1,000	150	600	..	1.025	34
3	1,000	345	650	..	1.024	..
4	1,000	590	800	..	1.024	37
Totals	5,000	1,100	2,730	80	.....	..
	Total 6,100 cc.		Total output 2,810 cc.			
5	.....	1,500	310	..	.....	..

arteriosclerosis was present. Tissue removed at transurethral resection revealed carcinoma of the prostate, and subsequently he underwent bilateral orchiectomy and suprapubic cystotomy. After the second operation, he developed pain, coldness, and cyanosis in the right foot. A diagnosis of arteriosclerotic peripheral vascular insufficiency with impending gangrene was made, and the patient was transferred for amputation.

Laboratory

Urine

Routine: pH 5.0; S. G. 1.015; albumin and sugar negative; numerous R.B.C. and W.B.C. present

Max. 18 hr. conc. test 1.024

Urea clearance 38% 1 hr.
40% 2 hr.

Creatinine clearance, 130 L./24 hr.

Blood

Hemoglobin, 12.6 gm./100 cc.

W.B.C., 21,400

NPN, 23 mg./100 cc.

Serum creatinine, 1.0 mg./100 cc.

BUN, 12 mg./100 cc.

With the use of tetracaine hydrochloride spinal anesthesia, right supracondylar amputation was performed. Measured intake and output records are shown in Table 9 and Figure 7. Total intake was 7,660 cc., consisting of 6,000 cc. of 5% dextrose and 1,660 cc. of ice chips. During this same period the urine output was 6,945 cc., a measured excess of intake over output of but

655 cc. being achieved. The specific gravity of the excreted urine was high (1.024 or 1.025), and during the six-day period there was an increase of the NPN from 23 to 46 mg. per 100 cc. Under the conditions of this study the administered water was again apparently not adequate to prevent hyperconcentration of the urine and a sharply increased NPN. A measured excess of only 655 cc. intake over output would also strongly suggest that a negative water balance was induced during the study period.

The following patient (Case 6) was maintained on 4% rather than 5% dextrose postoperatively.

Case 6.—J. G. (U. H. #499957), a 73-year-old housewife, was admitted with a three-month history of diarrhea and rectal bleeding. Physical examination revealed a well-preserved, elderly

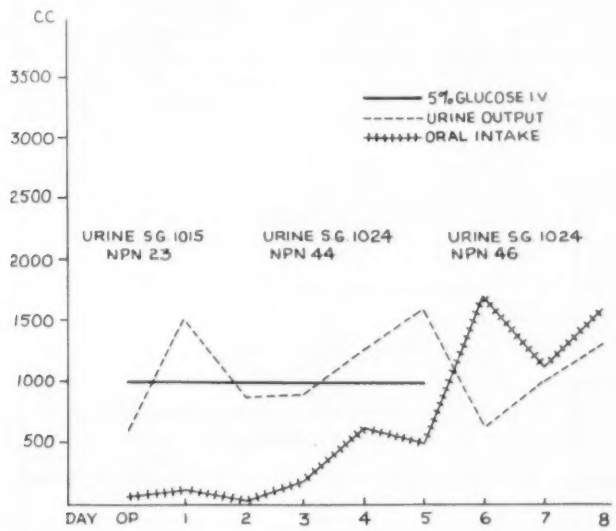

Fig. 7.—Postoperative intake and output record of Patient A. L. (#740515), aged 74, who had supracondylar amputation. (Reprinted by permission of W. B. Saunders Company; to be published in Surgical Forum Clinical Congress of the American College of Surgeons, W. B. Saunders Company, Philadelphia, 1954.)

Table 9.—*Postoperative Daily Measured Intake and Output Record Correlated with Urine Specific Gravity and Blood NPN (Patient A. L., U. H. #740515, Aged 74, Who Had Supracondylar Amputation)*

Postoperative Day	Intake, Cc.		Urine Output, Cc.	Urine S. G.	Blood NPN, Mg./100 Cc.
	5% Dextrose	Oral			
Day of operation	1,000	50	600	1.015	23
1	1,000	100	1,500	1.024	..
2	1,000	0	900	1.024	..
3	1,000	400	1,000	1.024	44
4	1,000	610	1,250	1.024	..
5	1,000	500	1,595	1.024	46
Totals	6,000	1,660	6,845	.....	..
	Total intake 7,660 cc.		Total output 6,845 cc.		

white woman. Height 5 ft. 1 in. (155 cm.), weight 120 lb. (54.4 kg.). Blood pressure 150/84, pulse rate 82, rate and rhythm regular. Significant findings were limited to a large neoplasm on the anterior wall at 8 cm. Biopsy revealed a somewhat undifferentiated adenocarcinoma.

Laboratory
Urine
Routine catheterized specimen showed occasional R.B.C. and W.B.C. per H.P.F.
Maximum 18 hr. conc. test 1.016
Urea clearance 95% 1 hr.
57% 2 hr.
Creatinine clearance 36 L. per 24/hr.
Blood
Hemoglobin, 13.5 gm.
W.B.C., 8,300 with normal differential count
Sodium, 141 mEq.
Potassium, 3.7 mEq.
Chloride, 103 mEq.
CO_2, 58 vol. %
NPN, 23 mg./100 cc.
BUN, 7 mg./100 cc.
Fasting sugar, 73 mg./100 cc.
Total proteins, 5.8 gm./100 cc.
Albumin, 3.7 gm./100 cc.
Globulin, 2.1 gm./100 cc.
A/G, 1.8
Prothrombin time, 100%
Kahn, negative
Stool
4+ guaiac

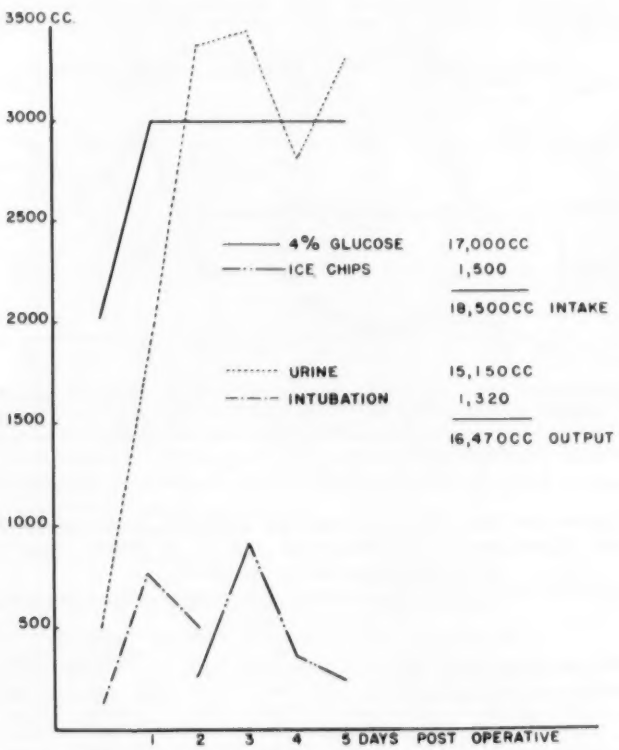

Fig. 8.—Intake and output record of Patient J. G. (#499957), aged 73, who had combined abdominal-perineal resection of the rectum.

A one-stage combined abdominal-perineal resection of the rectum was performed with the use of intratracheal N_2O-O_2-ether anesthesia. During operation 1,500 cc. of blood was transfused. Measured intake and output records are shown in Table 10 and Figure 8. Total intake for the

six postoperative days was 18,600 cc., consisting of 17,000 of 4% dextrose and 1.500 cc. of ice chips. Urine output for this same period was 15,150 cc. of low specific gravity (1.005 or 1.006). Another 1,320 cc. was lost by gastric suction during the first three days. Loss of body fluid through the posterior wound was not estimated. When the uncalculated variables of

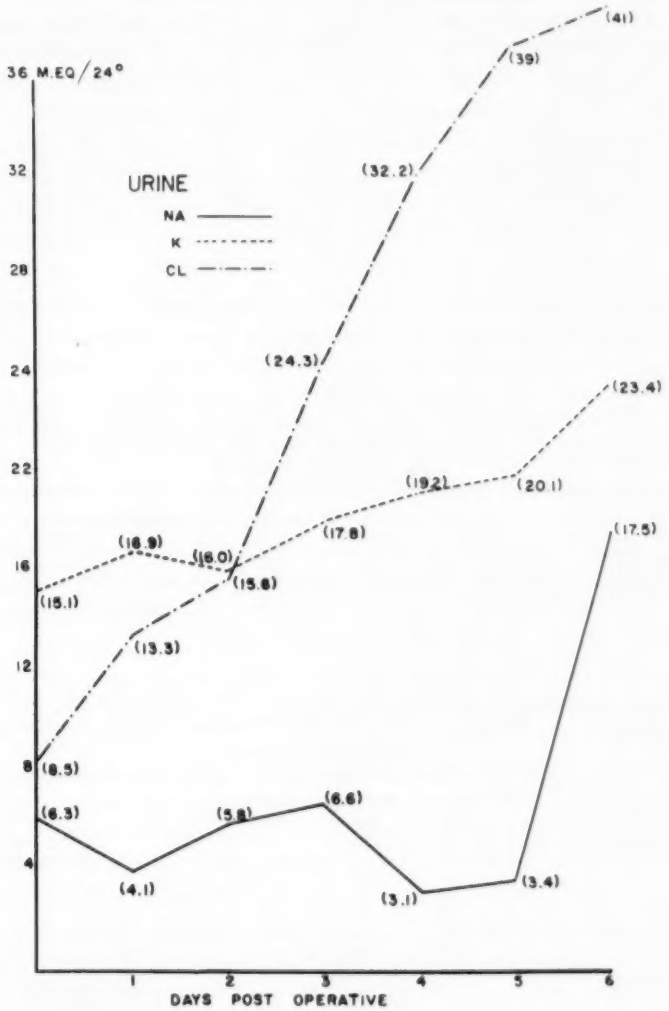

Fig. 9.—Chart showing postoperative urinary excretion of sodium, potassium, and chloride in Patient J. G. (#499957), aged 73, who had combined abdominal-perineal resection.

insensible loss, preformed water of metabolism, and posterior wound drainage are taken into consideration, this patient was probably in negative water balance for the period of study. At no time, however, were clinically identifiable deleterious effects of such large volumes of intravenous solutions observed.

Serum electrolyte levels before operation, the day following operation, and at the end of the six-day study period are shown in Table 11. Sodium levels remained fairly constant, while potassium and chloride showed constant fall. There was an increase in the CO_2 content from 58 to 75 vol. % at the end of the study.

TABLE 10.—*Postoperative Daily Intake and Output Record of Patient J. G., U. H. #499957, Aged 73, Who Had Combined Abdominal-Perineal Resection of the Rectum*

	Intake, Cc.		Output, Cc.	
Postoperative Day	4% Dextrose	Oral	Urine	Gastric Suction
Day of operation	2,000	...	500	150
1	3,000	60	1,900	720
2	3,000	250	3,300	450
3	3,000	890	3,400	...
4	3,000	300	2,800	...
5	3,000	0	3,250	...
Totals	17,000	1,500	15,150	1,320
	Total intake 18,600 cc.		Total output 16,450 cc.	

TABLE 11.—*Blood Chemistries Before and After Administration of 17,000 Cc. of 4% Dextrose (Patient J. G., Aged 73, Who Had Combined Abdominal-Perineal Resection of the Rectum)*

	Sodium, mEq.	Potassium, mEq.	Chloride, mEq.	CO_2, Vol. %
Before operation	141	3.7	103	58
Day following operation	137	2.8	87	65
6th postoperative day	140	2.7	84	75

TABLE 12.—*Postoperative Urinary Excretions of Sodium, Potassium, Chloride, and Dextrose (Patient J. G., #499957, Aged 73, Who Had Combined Abdominal-Perineal Resection of the Rectum)*

Postoperative Day	Sodium, mEq.	Potassium, mEq.	Chloride, mEq.	CHO, Gm.	Comment
Day of operation	6.3	15.1	8.5	0.3	1,500 cc. blood given during operation
1	4.1	16.9	13.3	0.8	.....
2	5.8	16.0	15.6	1.2	.....
3	6.6	17.8	24.3	3.8	.....
4	3.4	20.1	39.0	1.0	.....
5	3.1	19.2	32.2	0.1	.....
6	17.5	23.4	41.0	0.0	1,000 cc. Hartmann's solution given
7	85.0	27.8	92.0	0.0	Oral feedings resumed
8	92.0	23.0	94.0	0.0	.....

Urinary excretion of sodium, potassium chloride, and dextrose are shown in Table 12 and Figure 9. Sodium showed the same remarkable conservation observed in patient E. M. (Case 3). Chloride excretion rose progressively during the postoperative period. There was also gradual increase in potassium excretion. Less than 1% of the administered dextrose was excreted in the urine, as only 6.4 gm. of the infused 680 gm. was lost in this manner.

After the colostomy was revised, this patient was discharged in good physical condition.

COMMENT

It had long been observed that certain elderly patients, maintained postoperatively on 5% dextrose and water solution, had but a few cubic centimeter recorded difference between daily intake and output. On oral fluids, however, the ratio of intake to output would increase. To better understand this response, large volumes of intravenous water, far in excess of ordinary needs, initially were given to observe tolerance and whether or not significant hypo-osmolar (water-intoxication) symptoms could be induced. Aged patients seem quite capable of taking care of large amounts of intravenous dextrose solutions if they have reasonably good renal function. No clinically deleterious effects were noted from such stress. There were, however, mild to moderate signs of interstitial volume depletion at the end of all study periods. Large volumes of intravenous water and dextrose solutions can produce a negative water balance, and such was observed in certain of these cases. This observation had been previously well documented.[10]

Two patients, each 87 years old (Cases 1 and 2), showed good tolerance to large volumes of intravenous water. Diuresis was well established 24 hours following operation. Large amounts of urine of very low specific gravity were excreted by both patients, but the handling of such large loads of water was quite different when the intake-output records are compared. Patient I. S. (Case 1) was in negative water balance at the end of the study period, as his urinary output exceeded intravenous intake by 100 cc. (Table 2). Patient J. S. (Case 2), however, had an excess of 4,290 cc. of intake over output over a comparable period of time and under similar environmental circumstances. An average of about 700 cc. daily difference between measured intake and output could conceivably represent water contributing importantly to insensible loss.

The difference in handling of such intravenous fluids in these two patients emphasizes the fallacy in establishing "standard rules" for postoperative fluid administration. It is essential that each patient be individualized as regards his response to all constitutents of a given supporting fluid. "Adequate" postoperative urine output, particularly in elderly patients, does not necessarily mean that water needs have been satisfactorily met during a period of parenteral fluid administration. Careful correlation of all qualitative and quantitative factors of intake with urine output is necessary to determine whether or not a reasonable amount of water has been made available for insensible loss.

Two patients (L. S., Case 4 and A. L., Case 5) were maintained for five and six days, respectively, on 1,000 cc. of 5% dextrose daily and ice chips. Both patients excreted urine of high specific gravity and demonstrated increasing blood NPN (Figs. 6 and 7). Patient L. S. (Case 4) had an excess measured intake over output of 3,290 cc. for a five-day study period, an average of 600 cc. a day. When oral intake was resumed, only 310 cc. of urine was excreted in response to a 1,500 cc. intake, again probably representing water loading to compensate for deprivation during the study period and the administration of intravenous dextrose. It is of interest to observe that on the prevous day 800 cc. of urine was excreted in response to an intake of 1,590 cc., of which 1,000 cc. was intravenous 5% dextrose in water.

The response of patient A. L. (Case 5) was unusual. This man had undergone previous transuretheral resection, suprapubic cystotomy, and bilateral orchiectomy. It was thought that he probably would be unsatisfactory for this study, until it had been established that maximum renal concentration was 1.024 and that creatinine clearance was 130 L. per 24 hours. The urea clearance was only 40%, however. This patient had but an 815 cc. excess of intake over output for a six-day study period, a daily average of 135 cc. High urine specific gravity (1.024) and a sharp increase in NPN were observed despite a relative large urine output. He apparently was in negative water balance during the administration of intravenous fluid. Preexisting urinary-tract disease could conceivably have importantly contributed to this unique response.

The daily volume of 5% dextrose was decreased to an average of 2,100 cc. for six postoperative days in Patient E. M. (Case 3; Fig. 4, Tables 5 and 6). Because of a 1,700 cc. loss of gastric contents by suction in the first 48 hours, 500 cc. of Ringer's solution was given on the second postoperative day to partially cover this loss. Over-all excess of intake over output during this period was only 900 cc., an average of 150 cc. per day. A negative water balance was the net result. Serum sodium, potassium, chloride, CO_2, and NPN were lower at the completion of the period of intravenous fluid administration than preoperatively. No clinical effects of decreased osmolarity were observed.

Studies of the postoperative excretion of urine electrolyte demonstrated good renal conservation of sodium (Fig. 5, Table 7). Potassium excretion fell gradually, except for a small increase following the administration of 500 cc. of Ringer's solution.

Patient J. G. received 4% instead of 5% dextrose solution during the postoperative period (Fig. 8, Table 10). This was done to observe tolerance and to determine whether or not a less concentrated dextrose solution would produce greater water retention. During the first six postoperative days measured excess of intake over output was 2,030 cc., the daily average being 340 cc. Although well tolerated, it is improbable that this covered insensible and posterior wound loss and a negative balance was again achieved.

Serum electrolyte determinations (Table 11) revealed the sodium level essentially unchanged by such a stress. Potassium levels fell progressively, and CO_2 rose from 58 vol. % preoperatively to 75 vol. % at the end of the six-day period. There was a concomitant fall in serum chloride. Tendency towards alkalosis with progressively increasing urine chloride and potassium is of interest and coincides with falling serum chloride and potassium levels. Most kinds of diuresis are associated with loss of potassium. Potassium loss is associated with chloride loss at least until the cation and anion losses are marked.† Although this mechanism remains poorly understood, alkalosis and relatively high urine chloride observed in this patient were probably due to potassium loss induced by diuresis.

The ability of the kidney to conserve sodium in the face of such diuresis undoubtedly prevented the onset of symptoms of severe extracellular fluid volume deficit in spite of loss by gastric suction and continued loss from the posterior wound. A

† References 11 and 12.

TABLE 13.—*Preoperative and Postoperative Blood and Extracellular Fluid Volumes*

Patient	Height	Weight, Lb.	Age, Yr.	Operation and Internal Fluids	When Done	Hemoglobin, Gm./100 Cc.	Hematocrit	Protein, Gm./100 Cc.	Serum, Ml.	R. B. C., Ml.	Total Blood Volume	Extracellular Fluid Volume
I. P.	5'1"	122	71	Sigmoid resection	Preop.	14.7	41.3	6.79	2,351	1,403	3,754	8,435
				Interval fluids: 1,000 cc. whole blood	15 hr. postop.	15.0	37.5	6.45	2,519	1,284	3,803	9,400
M. S.	4'11"	159	76	Ventral herniorrhaphy	Preop.	15.6	41.5	6.22	2,104	1,269	3,373	8,075
				Interval fluids: 15,500 cc. 5% dextrose; 300 oral	8 days postop.	15.5	42.9	5.23	3,165	1,383	3,548	8,747
C. S.	5'2"	108	79	Gastroenterostomy and vagotomy	Preop.	11.7	32.3	6.84	2,639	1,368	3,707	14,132
				Interval fluids: 1,000 cc. blood; 5,000 cc. 5% dextrose	3 days postop.	13.6	38.5	6.49	2,175	1,155	3,330	.....
I. S.	5'6"	120	87	Inguinal herniorrhaphy	Preop.	13.3	36.6	6.59	2,732	1,340	4,072	.....
				Interval fluids: 2,000 cc. 5% dextrose	15 hr. postop.	12.7	35.9	6.36	2,585	1,234	3,818	11,092
E. M.	5'4½"	100	72	Gastric resection	Preop.	15.3	44.8	5.93	2,452	1,693	4,147	16,600

fivefold increase in urine sodium was observed on the seventh postoperative day after infusion of 1,000 cc. of Hartmann's solution. With the resumption of a normal food intake, a rapid return to preoperative values was observed (Table 12).

Data from a small number of patients (Table 13) revealed that blood volumes tended to be somewhat lower than accepted norms. There was no apparent significant effect upon blood volume produced either by operation or by large loads of 5% dextrose. Patient C. S. had a 500 cc. drop in serum volume after three days of intravenous dextrose therapy. This was undoubtedly related to a considerable amount of fluid lost by gastric suction after gastroenterostomy and vagotomy. Extracellular fluid volumes were variable and inconclusive.

SUMMARY AND CONCLUSIONS

Varying loads and concentrations of dextrose and water have been administrated to patients over 70 years of age.

Large amounts of intravenous dextrose and water (up to 3,000 cc. daily) were well tolerated. A negative water balance was observed in certain patients, however.

Under conditions of this study, 1,000 cc. of intravenous 5% dextrose and water daily, implemented by minimal oral fluid intake, did not prevent hyperconcentration of the urine and gradually increasing NPN.

Careful evaluation is necessary in order to determine the significance of an "adequate" postoperative urine output in patients being maintained on intravenous fluids. A large urine output may actually be masking a negative water balance. Correlation of intake and output is absolutely essential.

Observed renal conservation of sodium in two patients was excellent. Both patients tolerated considerable extracellular fluid depletion without significant clinical symptoms.

Large volumes of 4% dextrose were administered postoperatively to one patient. They were well tolerated. The significance of serum electrolyte levels and urine electrolyte excretion as observed in this patient has been discussed.

Because of individual tolerances to intravenous fluids, an ideal volume for routine administration to elderly patients cannot be recommended. The majority, however, seem to do well on 1,500 to 2,000 cc. a day, provided that it is given slowly.

Oral fluids are handled with greater efficiency and the sooner that patients in this age group are returned to oral feedings the better.

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METABOLIC ALTERATIONS IN SURGICAL PATIENTS

IV. Electrolyte, Water, and Nitrogen Balance Studies in Patients with Obstruction of the Pylorus or Small Intestine

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O'SHAUGHNESSY [1] in 1831 reported that the blood of patients with cholera had a reduced water content and was deficient "in salts, especially the carbonate of soda." He also emphasized that the blood urea increased when a suppression of urine occurred. A short time afterward, Latta,[2] who learned of these observations, gave a salt solution orally to a patient with cholera but found that it increased the vomiting and diarrhea. He then injected a warmed salt solution intravenously and reported a dramatic, although temporary, improvement in a moribund patient with cholera.

In 1852 Bidder and Schmidt [3] published the results of their extensive studies concerning the secretions of the gastrointestinal tract and the associated digestive glands. Their work in the normal person demonstrated that large quantities of fluid with a fairly uniform total solute content were secreted into the alimentary tract and subsequently were almost completely reabsorbed. These findings were applied by Schmidt [4] in treating patients suffering from dysentery and cholera. The observations of Bidder and Schmidt were among the early important contributions which subsequently lead to our understanding of changes in body fluid resulting from a loss of gastrointestinal secretions or a translocation of fluid into the bowel. Barlow,[5] in 1844, and Brinton,[6] in 1867, demonstrated that patients with intestinal obstruction showed evidence of extreme water loss comparable to that resulting from cholera. Brinton also showed that the rate of loss of these important constituents can be greatly accelerated by giving food and fluid to patients with obstruction. He produced obstruction of the intestine by tying a heavy cord around the bowel in dogs and then offered them food and water. He remarked that "one animal drinks

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eagerly, distends its stomach, vomits frequently, and dies in a day or two. Another, to all appearance, in exactly the same state of health, drinks little, distends but slightly, vomits not at all and lives for almost as many weeks." In discussing the treatment of intestinal obstruction, he states, "the avoidance of distention is to be attempted by reducing, in every available way, the quantity of food and drink, restricting the latter to small sips of cool liquids." After this, little knowledge was gained concerning the metabolic alterations resulting from either high or low gastrointestinal obstructions until the early part of the 20th century. In 1912 Hartwell and Hoquet [7] showed that dogs with a high obstruction could be kept alive for weeks if isotonic sodium chloride solution was injected subcutaneously. MacCallum [8] showed that hypochloremia and increased alkali reserve occurred in animals with pyloric obstruction. It remained for the important and classic experiments of Gamble and Ross [9] and Gamble and McIver [10] to demonstrate the fluid and electrolyte losses which occurred after an experimentally produced pyloric obstruction. These workers also found that the loss of sodium, rather than chloride, was the decisive factor in determining the extent of dehydration, since the organism can compensate for a decrease in chloride ion by increasing the bicarbonate content of the body fluids. While dehydration was apparent in patients with obstruction of the small intestine, the finding of relatively normal values for hemoglobin, hematocrit, and plasma solute concentrations erroneously led to the belief that dehydration and an electrolyte deficiency contributed little to the cause of hypotension, oliguria, and death.[11] This concept prevailed even though McIver and Gamble [12] had pointed out in 1928 that the loss of bile and intestinal fluid containing approximately the same amount of fixed base (chiefly sodium) and chloride as does plasma may occur and thus a normal ionic concentration tends to be sustained at the expense of a reduction in volume. Since Gamble and his co-workers * have shown that sodium and chloride are of chief importance in maintaining the volume of the blood plasma and interstitial fluid, and because these two substances are the major electrolytes of the digestive secretions, anything which interferes with their reabsorption should result in a diminished extracellular space. They also emphasized that dehydration resulting from the loss of gastrointestinal fluid cannot be repaired with water alone and that a restoration of the lost electrolytes is essential. Foster,[13] in 1928, showed that in animals with obstruction the loss of gastrointestinal fluid was increased when liquids were taken orally because secretion continued with inhibition of reabsorption. He also demonstrated that a starved dog with a simple intestinal obstruction had a survival time comparable to that of starved dogs without obstruction. He found that parenteral administration of an isotonic sodium chloride solution prolonged this survival time. Butler, McKhann, and Gamble,[14] in 1933, while studying the fluid and chemical losses of infants dehydrated from diarrhea, found that appreciable quantities of intracellular fluid, potassium, and phosphate were lost concomitantly with a diminution of extracellular constituents.

Raine and Perry [15] believed that moderate degrees of distention increased intestinal peristalsis and secretion but diminished reabsorption. They thought it was unlikely that toxic substances were absorbed and attributed the symptoms and death of animals with low intestinal obstruction to the loss of fluid, sodium, and chloride. Herrin and Meek,[16] in 1933, demonstrated that distention of an intestinal loop

* References 9, 10, and 12.

resulted in the following changes: an excessive secretion, a loss of both water and chloride from tissues, a decreased blood and plasma volume, elevations in the nonprotein nitrogen and hemoglobin contents of the blood, and alterations in both the alkaline reserve and the chloride content of the serum. While subsequent studies [17] showed that a decreased capillary blood flow and diminution in the secretion of gastrointestinal juices existed when intestinal distention was marked, it seems apparent that the physiological alterations are dependent on the degree of pressure within the intestinal lumen. Moderate pressure causes increased secretion and interference with reabsorption, while further increases of pressure reduce or shut off the capillary blood flow and secretion stops. Surprising quantities (1,000 to 8,000 ml.) of fluid may accumulate in the gastrointestinal tract and peritoneal cavity and will not be reabsorbed until the distention or inflammation subsides. Subsequent studies by Aird,[18] Gendel and Fine,[19] and Fine, Hurwitz, and Mark [20] confirmed the findings that distention of the intestine per se will cause a marked decrease in blood and plasma volume. Gatch and Battersby [17] found that in continued distention, the intestinal wall exuded into the peritoneal cavity a fluid which contained from 3 to 4 gm. of protein per 100 ml., most of which was albumin. After the distention was relieved, the bowel wall became edematous. Abbott, Mellors, and Muntwyler† reported 20 to 40% reductions of the plasma volume and sizeable losses of the thiocyanate space in dogs with simple pyloric, ileal, or colonic obstructions. Ender and Herrin [23] substantiated this work, in 1945, by showing a 23 to 29% decrease in plasma volume and proportional losses in the extracellular fluid volume following experimentally produced intestinal obstruction in rabbits. Recently, Ellison, Zollinger, Cedars, and Britt [24] reported an average blood volume deficit of 1,200 cc. in 27 patients hospitalized with intestinal obstruction. They state that the plasma loss in these patients exceeded the red cell loss and varied directly with the duration of obstruction. When the obstruction was present one to two days, there was a 27% decrease, and three to four days, a 37% deficit of the plasma volume. While the role of bacteria and their metabolic products has been well demonstrated in closed-loop obstruction and strangulation,‡ the loss of body fluid and electrolytes are also of great importance in these two types of obstruction, as well as in simple intestinal obstruction and adynamic ileus.

Because of the significance of fluid, electrolyte, and nutritional alterations on the clinical course of pyloric and low small bowel obstruction this study was undertaken. Our objectives were as follows:

(1) To determine, by means of metabolic balance techniques the alterations in water, sodium, potassium, chloride, and nitrogen metabolism resulting from either high or low obstructions of the gastrointestinal tract

(2) To gather more information concerning the composition of the fluid lost through the gastrointestinal tract

(3) To determine whether there were any changes in the composition of gastrointestinal fluid which were dependent on the disease or type of therapy employed

(4) To estimate the magnitude of various constituents which might be temporarily translocated into the intestinal wall or lumen or into the peritoneal cavity.

† References 21 and 22.

‡ References 25 and 26.

METHODS

Included in this report are two main groups of cases: (1) patients exhibiting pyloric obstruction and (2) patients with obstruction of the terminal ileum. In the first group, six patients exhibited varying degrees of pyloric obstruction. In two of the patients, J. S. and W. B., the obstruction was partial and transitory, while in four patients, S. A., F. U., H. L., and D. B., it was complete or almost complete. In patient F. U. the obstruction was almost complete, though temporary, and with subsidence of edema and spasm, he was able to take an adequate diet orally six days after admission to the hospital. The second group includes six patients (M. K., A. W., W. G., P. J., W. S., and W. M.) with ileal obstruction and an additional patient, S. M., who had roentgenological findings of ileus, although the cause of this was not determined. Four of these patients were operated upon within 6 to 20 hours after admission, and the two remaining patients (P. J. and S. M.) were treated by conservative measures.

All patients were studied on the Surgical Metabolic Division of the University Hospitals of Cleveland. Methods for the analysis of all nutrients, parenteral and oral, and excreta (urine, feces, gastrointestinal or wound drainage, emesis, and sputum), as well as the methods of carrying out the balance studies, have been previously described.[27]

The results of the balance study are chartered by plotting the intake, the output, and the balance as the ordinate and the time (24-hour periods) as the abscissa. The intake is plotted upward from the horizontal zero line and the output from the top of the intake column downward. A positive balance is shown by the clear white area above the zero line. When the output stops at the zero line, equilibrium is attained, while extension of the column below this line represents a negative balance. All patients were given vitamins § intravenously or orally in amounts sufficient to exclude the metabolic effects of any possible vitamin deficiency. The nitrogen, sodium, potassium, and chloride content of the whole blood given was determined,‖ but since the rate of entrance of the various constituents of blood into the metabolic pool is not precisely known, and since it was given in amounts approximating that lost during the operation, it was represented by the broken-line extension of the intake column. The balance that would have occurred if blood was included is shown by the broken horizontal lines in the sodium, chloride, potassium, and nitrogen columns. Because the insensible water loss cannot be accurately determined, it was represented by a broken horizontal line 1,000 ml. below the other measurable excreta in the chart depicting water balance. While some variations from this estimated figure undoubtedly occurred, it is believed that the inclusion of the insensible loss provides a more accurate balance.

RESULTS

In Figures 1 (Patient H. L.) and 2 (Patients W. B., J. S., F. U., S. A., and D. B.,) are shown the results obtained from the study of five men and one woman with pyloric obstruction due to peptic ulcer. Large amounts of gastric fluid were removed from all patients in this group except Patient W. B., which accounted for the negative water balance for the first four to seven days. In patients with an active ulcer in whom gastric suction is employed, greater losses of chloride than sodium occurred. Patients without an active ulcer show an equal loss of sodium and chloride from this source. From these and other studies, it seems apparent that there is a conservation of chloride so that in a day or so only a few milliequivalents appear in the urine. The conservation of chloride not only occurs more rapidly but to a greater extent than that of sodium or potassium if an inadequate intake of these two ions exists, or if they are being lost in excess of chloride. It is also evident from these studies (Patients H. L., F. U., S. A., and D. B.) that when large quantities of chloride are lost by vomiting or drainage a considerable amount of fixed base is excreted

§ Solu-Zyme and Unicaps furnished by The Upjohn Company, Kalamazoo, Mich.

‖ Blood obtained from the blood bank had the following average composition: sodium 91.7 mEq., potassium 36.2 mEq., chloride 65.3 mEq., and nitrogen 17.5 gm. per liter.

by the kidneys in an attempt to maintain osmotic equilibrium. In spite of the fact that Patient H. L. received approximately 775 mEq. of potassium and 860 mEq. of sodium during the first seven days of study, he still developed the following cumulative deficits: 180 mEq. of potassium, 585 mEq. of sodium, and 1,135 mEq. of chloride. It is interesting to note that he was given 906 mEq. of chloride intravenously during the first seven days and lost 1,933 mEq. in the gastric juice, 105 mEq. in the urine, and 14 mEq. in the stool during this period. Since this patient received 3 liters of 5% dextrose in isotonic sodium chloride (465 mEq. of sodium and chloride) the evening prior to the start of the study, the deficit was not as large as indicated. In contrast, his urine sodium loss amounted to 763 mEq., as compared with 675 mEq. lost though the gastric secretions over this same period. His serum electrolyte values are shown in Table 1.

While the cumulative potassium losses were not large in Patients H. L. (180 mEq. in seven days) and S. A. (140 mEq. during the first five days), they both

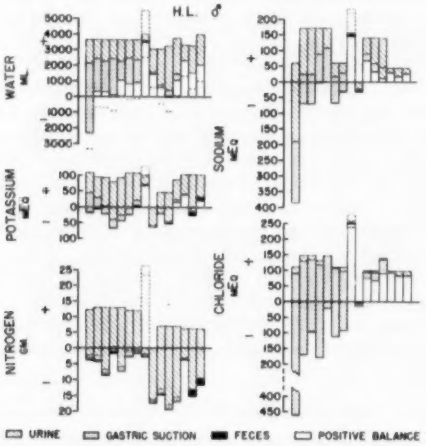

Fig. 1.—Metabolic balance studies in a patient with pyloric obstruction. Hemigastrectomy-vagotomy was done on the eighth study day.

showed electrocardiographic changes indicative of severe electrolyte imbalances which were rapidly alleviated by the slow intravenous administration of 80 to 100 mEq. of potassium. Because of the severity and duration of obstruction in these two patients, who had had a marked weight loss prior to their admission, it was believed that they had lost considerable potassium prior to entering the hospital; consequently, further relatively small losses led to the changes observed. Patient H. L. showed a retention of sodium and chloride postoperatively out of proportion to what we have noted in other patients, presumably due to the large preoperative deficits of these ions. In contrast with Patient H. L., who showed a sizeable sodium deficit preoperatively, Patients J. S., F. U., and D. B. exhibited sodium retention prior to operation. During the first four to nine postoperative days these latter three patients had a small to moderate negative sodium and potassium balance. This may have resulted from a preoperative overloading with sodium. Sodium, chloride, and potassium were

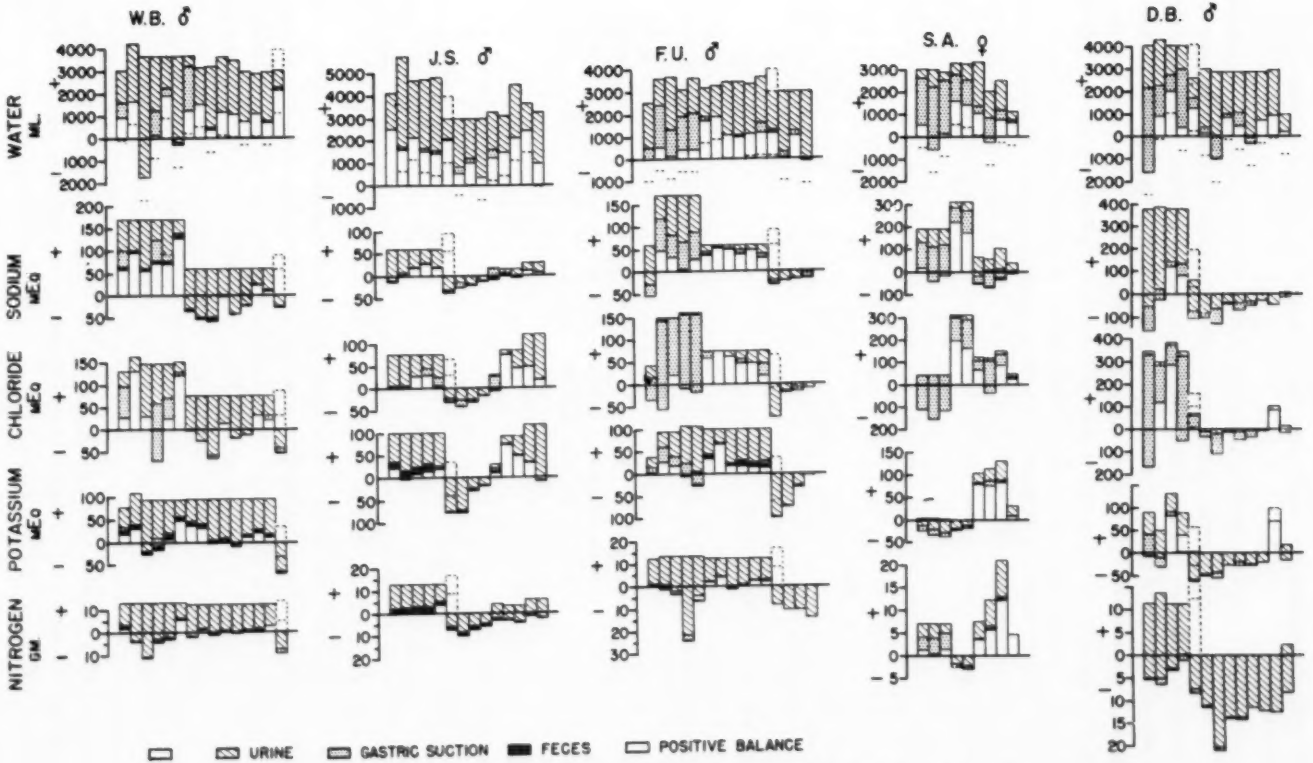

Fig. 2.—Metabolic balance studies in five patients with pyloric obstruction.

deliberately withheld from these three patients for the first four to seven days postoperatively so that the rate and extent of conservation of these cations could be determined.

The cumulative postoperative deficits of sodium, chloride, and potassium, and the resulting serum electrolyte changes are shown in Table 2. It can be seen that the deficit of potassium is quite comparable in these three patients. The sodium and chloride losses of Patient D. B. are in excess of that seen in the other two patients. Presumably, this is due to the extent of the preoperative overloading with sodium.

Sizable nitrogen losses occurred postoperatively in Patients H. L., J. S., F. U., and D. B. Studies were also done postoperatively in Patients W. B. and S. A., which are not presented in Figure 2. Their losses were slight in comparison with the four abovementioned patients. In fact, Patient S. A. showed a cumulative deficit of only 2.63 gm. of nitrogen over the first five postoperative days. However, because

TABLE 1.—*Serum and Electrolyte Concentrations Obtained from Patient H. L. During First Two Weeks of Study**

Study Day	1	6	7	8	10	13
Sodium, mEq./L.	139	142	136	132	131	136
Chloride, mEq./L.	101	82	...	83	85	94
CO_2 combining power, vol. %	...	...	84	83	79	57

* Operation was performed on eighth study day.

TABLE 2.—*Cumulative Deficits of Sodium, Chloride, and Potassium Observed in Patients J. S., F. U., and D. B., and the Effect on the Serum Concentrations of these ions*

Patient	Period of Cumulative Deficit	Sodium		Chloride		Potassium	
		Cumulative Deficits	Serum Conc., mEq./L.	Cumulative Deficits	Serum Conc., mEq./L.	Cumulative Deficits	Serum Conc., mEq./L.
J. S.	4	95	142-131	121	105-94	202	4.1-3.6
F. U.	4	69	136-136	119	100-95	204	4.8-4.1
D. B.	7	532	145-133	238	99-96	287	.....

she had been in a malnourished state for some time and received approximately 20 Cal. per kilogram of body weight a day with adequate minerals, she undoubtedly showed a greater retention of nitrogen than a vigorous patient would have exhibited after the same therapy and operative trauma.

The effect of dehydration and parenteral therapy on the chloride, sodium, and potassium concentrations of gastric fluid removed from Patient S. A. (also see Appendix for patient's hospital course) is shown in Figure 3. During the first three days, she received 191 mEq. of sodium and 44 mEq. of chloride orally, but since little of this was absorbed there were only slight changes in the electrolyte concentration of her gastric fluid. Her balance chart (Chart 2) shows the following cumulative deficit for the first three days: water 3,000 ml., sodium 40 mEq., chloride 383 mEq., and potassium 97 mEq. It can be seen that during the three days of dehydration she lost considerably more chloride than she ingested and the chloride concentration of gastric juice decreased slightly. The sodium and chloride levels increased when 2,000 ml. of a 5% solution of dextrose in isotonic sodium chloride was given intravenously for the next two days and the gastric-fluid loss diminished. The sodium concentration

of the gastric fluid rose to 80 mEq. per liter and the chloride concentration to 111 mEq. per liter. During the next two days, the sodium intake was considerably lower, accompanied by a high potassium chloride intake. During this period, the chloride concentration of the gastric fluid increased to 132 mEq. per liter. The potassium concentration, which had been falling during the period of dehydration and low potassium intake, rose to 10.3 mEq. per liter, while the sodium concentration fell to 63.5 mEq. per liter of gastric fluid. Finally, when dehydration again occurred with large chloride losses and a moderate sodium deficit, the concentration of both of these ions in the gastric fluid decreased.

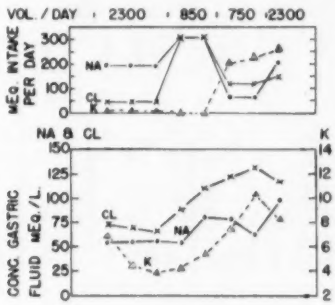

Fig. 3.—Effect of electrolyte intake and state of hydration on sodium, chloride and potassium concentration of gastric fluid. The average volume of gastric fluid drainage per day is shown at the top of the figure.

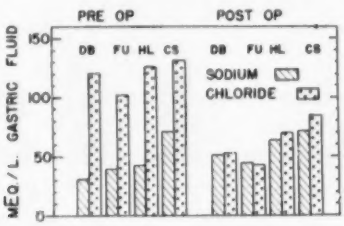

Fig. 4.—Changes in sodium and chloride concentration of gastric fluid obtained from four patients with peptic ulceration preoperatively and postoperatively.

In Figure 4 the concentration of sodium and chloride per liter of gastric fluid is shown in four patients with peptic ulcer (Patient D. B. with duodenal ulcer and Patients F. U., H. L., and C. S., with gastric ulcers), before and four days after operation (Patient D. B. had a gastroenterostomy-vagotomy, Patients F. U. and H. L. a hemigastrectomy-vagotomy, and Patient C. S. a 70% subtotal gastrectomy). It can be seen that postoperatively the sodium concentration of the gastric fluid increased slightly, while the chloride concentration showed a marked decrease in all four patients.

Figure 5 shows the results of metabolic balance studies of six patients with proved ileal obstruction (Patients M. K., A. W., W. G., P. J., W. S., and W. M.). The results of Patient S. M., who had marked distention of the large and small bowel from an unknown cause, are also included in Figure 5. In all patients, except

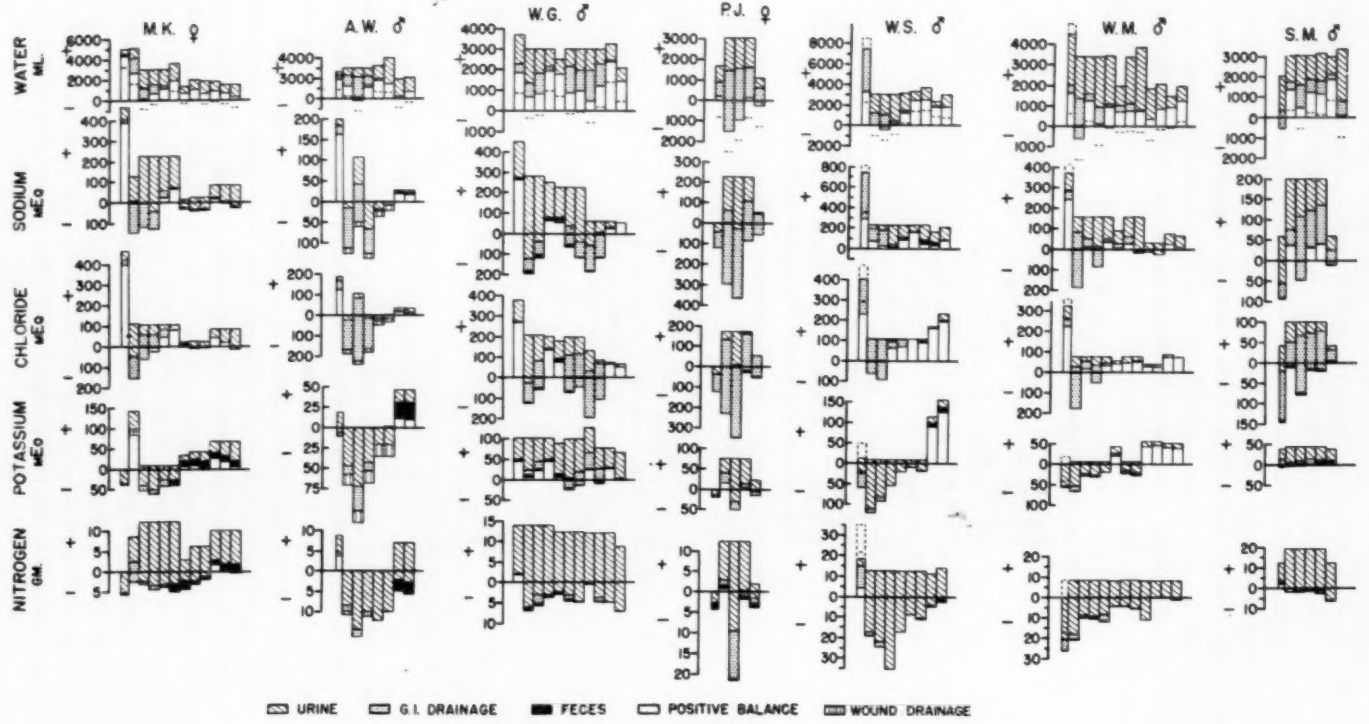

Fig. 5.—Metabolic balance studies in patients with small bowel obstruction.

Patients P. J. and S. M., who were not operated upon, a positive fluid, sodium, and chloride balance occurred during the first 18 to 36 hours. Thereafter, these balances were usually negative for several days, depending largely on the volume of gastrointestinal drainage and the parenteral fluid therapy. It will be noted that a negative chloride balance occurred after the first 24 hours, especially when there were large gastrointestinal losses. In four patients (M. K. after 36 hours, A. W. W. S., and W. M.) there were usually only small or trace amounts of chloride in the urine when significant gastrointestinal losses existed. In contrast, Patients W. G., P. J., and S. M. showed moderately large urinary chloride losses in spite of the fact they were losing fairly large quantities of this ion in the gastrointestinal drainage. The difference seen in these latter three patients is thought to be due to the fact that more equal losses of fixed base and chloride occur in patients with a tube in the lower portion of the small bowel than when the loss of fluid is from the stomach. Sodium losses in the urine were not as drastically curtailed, in Patient W. S., and after four and one-half days in Patient A. W., and on the last day or two in Patients W. G. and P. J. It should be noted that in the patients who were operated upon, notably Patients M. K., A. W., W. G., W. S. and W. M., moderately large amounts (160 to 400 mEq.) of sodium were retained during the first 24 hours.

Patients A. W., W. S., and W. M. were given only small amounts of potassium for the first five to seven days of the study. It is interesting to note that these patients also exhibited the largest nitrogen deficits in spite of the fact that Patients W. S. and W. M. were given 9 to 12.2 gm. of nitrogen, as amino acids, intravenously per day. Patient A. W. received only 600 Cal. daily in the form of a 5% dextrose solution and an adequate potassium intake. In this patient, the wound drainage, which was not profuse, contained from 10 to 25 mEq. of each, sodium, chloride, and potassium daily. Although Patients W. S. and W. M. were given 1,000 to 1,200 Cal. a day, intravenously, their nitrogen deficits for the first five days were the largest noted in this group. Patients S. M. and P. J. (except for the third day of study), who were not operated upon and had the largest caloric intake, showed the smallest nitrogen losses.

In these patients, it is of interest to note the large sodium and chloride losses that result from gastrointestinal drainage. For example, on the second and third hospital days, Patient P. J. lost an average of 343 mEq. of sodium and 288 mEq. of chloride daily in the gastrointestinal drainage. In Patient W. S. the small intestine was so distended that it was believed unwise to resect the strangulated necrotic segment without first decompressing the intestine. Since the volvulus had occurred around a Meckel diverticulum, the bowel was drained through an opening made in this structure. This allowed removal of a moderate amount of gas and 3,580 ml. of fluid which had accumulated in the small bowel. The necrotic bowel and the diverticulum were then resected. While this represents a considerable translocation of fluid and electrolytes, the amount which remained in the lumen of the bowel and that which was evident as edema must have been equally as large. Since this fluid is rich in protein and had an electrolyte concentration essentially equal to that of the extracellular fluid, from which it was derived, it is apparent why this patient, who 14 hours before was a healthy active person, was subsequently in such a serious state.

Since the obstruction and distention was relieved in a few days in many of these patients, the long intestinal tube was removed before it reached the lower portion of the small intestine. In Patient S. M. it reached the terminal ileum, and it is important to appreciate the changes in the sodium and chloride concentrations of the gastrointestinal fluid as the tube progressed downward. The first day that the tube was in the stomach the concentration of sodium was 40 mEq. and chloride 129 mEq. per liter of fluid. The next morning it had entered the jejunum, and the sodium was then 88 mEq. and the chloride 132 mEq. per liter. A few days later, when it entered the lower portion of the terminal ileum, the concentration of sodium increased to 136 mEq. and the chloride fell to 96 mEq. per liter of ileal fluid, at which time his serum sodium concentration was 140 mEq. and chloride 100 mEq. per liter.

COMMENT

The results of our studies in patients with pyloric obstruction are in agreement with earlier reports.¶ It is evident that the loss from the stomach of large amounts of fluid, rich in chloride, leads to an excretion of fixed base in the urine. It is also apparent that in patients with an active peptic ulcer the loss of sodium by way of the kidneys may constitute from 60 to 90% of the total sodium loss. This is well exemplified by patients H. L., D. B., and F. U. In nonulcer patients or in older patients who have an obstructing carcinoma or a stenosis resulting from scar tissue of an inactive chronic ulcer, the loss of sodium in the gastric fluid may constitute upward of 50% of the total sodium loss (Patient S. A.) In studying the source of the losses of chloride and water, it is evident that an opposite situation from that of sodium exists. In such circumstances the patient with an active ulcer loses from 50 to 95% of the total chloride by way of the gastric drainage or vomitus, and almost insignificant amounts of chloride appear in the urine and stool. Large fluid losses may also occur from the excessive gastric secretion of patients with an active peptic ulcer. Instead of conserving water and reducing the volume of urine, such patients, especially during the first few days, excrete moderately large quantities of fluid and fixed base by way of the kidneys in an attempt to maintain a normal ionic concentration and rid the body of nitrogenous waste products. Thus, early in the course of such an illness, little alteration from the normal chemical concentrations of the various constituents of blood exist, since water is provided from both the extracellular and intracellular compartments, enabling the kidneys to excrete the solutes which are accumulating in excessive amounts. When dehydration and an inadequate caloric intake coexist, the catabolism of body tissue increases to provide energy and additional water.

Elkinton and Taffel [29] pointed out that with prolonged dehydration and starvation there is a greater loss of potassium than that derived from the breakdown of tissue. Thus, the cellular constituents (protein and potassium) enter the extracellular compartment in increasing amounts. The results of these workers are comparable to the studies of Butler, McKhann, and Gamble,[14] who reported this phenomena in 1933 and concluded as follows: "It thus seems that potassium and a corresponding

¶ References 9, 10, 12, and 28.

quantity of intracellular water are excreted in the urine to a much greater extent than can be accounted for by the destruction of body protoplasm." The results of our present and past studies [27] substantiate these observations.

If the loss of gastric secretions continues and little additional water is available, a hypochloremia, increase in the alkaline reserve, and oliguria occur. The urine usually has a high specific gravity, but if renal damage existed previously, or develops, the urinary specific gravity may fall, with the appearance of varying amounts of albumin and cells. The concentration of nitrogenous waste products and frequently potassium then increases in the blood.

We now know that many factors may influence this chain of events. Our findings corroborate previous work # which showed that patients with peptic ulcer usually have much higher concentrations of chloride and smaller quantities of sodium in gastric juice than do normal persons or patients with carcinoma of the stomach. Thus, patients with an active peptic ulcer are likely to show a more profound alkalosis and exhibit a larger urinary loss of fixed base than that which occurs in nonulcer patients.

It has been pointed out frequently, over the course of many years,* that when an obstruction of the gastrointestinal tract exists the oral ingestion of fluid causes an increased loss of water and electrolytes and thus accelerates dehydration and acid-base imbalance. By permitting an oral intake while suction of the gastrointestinal tract is being employed, one not only makes the replacement therapy extremely difficult but usually aggravates the distention which the tube is attempting to alleviate. The giving of a solution intravenously, which is deficient in or free of electrolytes will not only fail to correct the abnormality [12] but it may further increase the loss of electrolytes through the kidneys. If the water and mineral losses can be minimized or replaced and sufficient calories provided, the catabolic phase may subside and thus reduce the amount of cellular constituents to be excreted.

In patients with an obstructing cancer of the stomach, alkalosis is rarely seen, although dehydration may be severe. This is usually a more chronic process, and thus the constituents of blood, interstitial fluid and intracellular space are all decreased concomitantly. Such patients frequently show blood counts and serum concentrations that are normal, although a marked deficit in the red cell mass, plasma volume, and cellular constituents exists.[34]

Randall [35] reported the average concentration of 130 specimens of gastric fluid to be as follows: sodium 59 mEq. (range 6 to 157 mEq.), potassium 9.3 (range 0.5 to 65.0) and chloride 89 mEq. (with a variation of 13.2 to 167.2 mEq.) per liter. Lans, Stein, and Meyer [30] gave the following values: Patients with pyloric obstruction due to a peptic ulcer had an average sodium of 56 mEq., and chloride 126 mEq. and potassium 12.6 mEq. per liter of gastric fluid. After vagotomy they found the average sodium concentration was 72 mEq., chloride 56 mEq., and potassium 12.1 mEq. per liter of gastric fluid. In their patients with pyloric obstruction due to carcinoma, the average sodium was 61 mEq., chloride 58 mEq., and potassium 10.2 mEq. per liter of gastric juice. Our results are in close agreement with those of the aforementioned workers and the more recent report of Ariel.[31]

References 30 and 31.

* References 6, 13, 32, and 33.

In discussing the alterations resulting from low intestinal obstruction it seems evident that large fluid and electrolyte losses can occur or that these constituents will be rendered temporarily unavailable to the normal metabolic pool in one or more of the following ways:

1. Omission of the normal fluid, electrolyte and nutritional intake. This plays a larger role if the patient is debilitated due to a chronic wasting disease or is not relieved of his obstruction within several days.
2. Losses of fluid and electrolytes.
   - (*a*) Insensible fluid loss
   - (*b*) Urinary loss
   - (*c*) Vomiting or the loss of fluid and electrolytes by gastrointestinal intubation
   - (*d*) Diarrhea (which occasionally may occur with partial intestinal obstruction; paralytic ileus, or during recovery).
   - (*e*) A temporary or permanent loss because of a translocation of significant quantities and electrolytes
     - (1) Increased catabolism of the body tissues
     - (2) A withdrawal of intracellular water and potassium in excess of that resulting from tissue breakdown
     - (3) Distention, which will result in edema and in intraluminal or peritoneal translocation of fluid and electrolytes
     - (4) Strangulation, with an accumulation or trapping of fluid, electrolytes, protein, and blood cells in the intestinal lumen or wall; edema of the mesentery and retroperitoneal tissues and intraperitoneal transudation of body-fluid constituents
     - (5) Infection, with exudation of fluid, protein, electrolytes, and blood cells

No single item in the outline presented above causes the peripheral circulatory collapse and death which occur as a result of various forms of intestinal obstruction, but it is a combination of factors, varying in extent from one patient to another, which leads to a blood volume deficit. It has been shown that bacterial invasion of the peritoneal cavity following a closed-loop or strangulated obstruction may cause a fatal sepsis. However, it is our belief that shock and death frequently occur from the marked translocation of fluid, protein, and electrolytes prior to the development of this fatal state. While it is impossible to assess the exact extent of all the individual factors contributing to the dehydration in patients with low intestinal obstruction, a knowledge of the approximate total magnitude of these losses and shifts is of paramount importance.

By adequate parental replacement therapy, the judicious use of gastro-intestinal intubation and antibiotics, and properly timed surgical intervention, the morbidity and mortality associated with this disease has been reduced.

SUMMARY AND CONCLUSIONS

By the use of metabolic balance techniques, marked fluid, electrolyte, and nutritional alterations were demonstrated in patients with pyloric or low intestinal obstruction. These changes have been discussed.

In general, patients with an obstruction high in the gastrointestinal tract lose considerable quantities of water and electrolytes (especially chloride) by vomiting or intubation and lose considerable amounts of fixed base in the urine. The effect of therapy on the electrolyte composition of gastric fluid was observed.

The external losses of fluid and electrolytes which occur following obstruction of the small intestine are easily measured, but unfortunately these losses may represent only a fraction of the total deficit. The internal shifts of fluid and electrolytes, which can at best be crudely estimated, are often overlooked, and yet they frequently are the major source of deficit.

The temporary or permanent loss of water and electrolytes (especially fixed base) in patients with obstruction results in alterations of other metabolic processes, which can be minimized or prevented by prompt and proper therapy.

Helene Banta and Laura Silver, dietitians; Christine Lane and Callie Burnside, dietitians' helpers; Dorothy Freymeyer, R.N.; Myrtle Edwards, R.N., Vida McKelvey, R.N., Kathleen Allen, R.N., Agnes Furman, R.N., Alice Stevulak, R.N., and also the laboratory staff, Jean Hower, Sophie Koenig, Ivan Madirazza, Doris Blum, Robert Gilman, Ingeborg Loesch, and Katherine Whiteside, and Evelyn Kocsis, secretary, aided in this study.

APPENDIX

H. L. (U. H. C. 652-580), a 43-year-old white man, was admitted on Nov. 9, 1953, with a diagnosis of peptic ulcer and a complaint of pain in the stomach. Fifteen years prior to admission the patient had a perforated ulcer which was plicated at another hospital. After this, he continued to have recurrent episodes of pain, nausea, and vomiting at irregular intervals. Two months prior to the present admission, the patient had almost continual epigastric pain and usually vomited daily. He had lost 20 lb. (9 kg.) during the two months prior to admission, and was admitted in acute distress, with severe epigastric pain and vomiting. Physical examination on admission was not remarkable, except for severe epigastric and right upper quadrant pain and the finding of a large ventral hernia at the site of the previous laparotomy. On the day of admission, the patient was given 3,000 cc. of 5% dextrose in saline and 1,000 cc. of 10% fructose in water. The following day balance studies were started and the patient given a daily intravenous regimen of 600 cc. of intravenous fat (Lipomul-I.V.†), 1,000 cc. of 5% protein hydrolysates (Amigen‡) in 10% fructose (Levugen), 1,000 cc. of 6% plasma hydrolysates (Travamin §) in 12% invert sugar and 1,000 cc. of 10% fructose in water. Potassium chloride, 68 mEq., was added to provide a total intake per day of 100 mEq. of potassium. This regimen was carried out on Nov. 10, 11, 12, and 13. On Nov. 14, the patient was given an oral intake regimen. The pyloric obstruction persisted, however, and the same intravenous regimen was resumed for another three days. On Nov. 17, the patient was taken to surgery where a hemigastrectomy-vagotomy with a Billroth-I type of anastomosis was performed. A departure from the original plan to give electrolyte-free fluids on the day of operation and the two succeeding days was necessitated by the patient's markedly delayed response following the administration of anesthesia and curare. After this failure to respond had prevailed for five hours, it was interpreted as reflecting a state of acute hypokalemia. This was confirmed by EKG, and he was given rapidly 40 mEq. of potassium chloride in 500 ml. of isotonic sodium chloride. This was followed by an additional 40 mEq. of potassium in 500 ml. of isotonic sodium chloride, more slowly, and finally the same evening he was given an additional 20 mEq. of potassium chloride in 1,000 ml. of 10% fructose. After the administration of 80 mEq. of potassium chloride, the patient began to respond from anesthesia rapidly (his respirations which had been assisted became voluntary), and his electrocardiogram showed a normal record. He was then main-

† Lipomul-I. V., a 15% vegetable oil emulsion containing 4.17% dextrose, furnished by the Upjohn Company, Kalamazoo, Mich.

‡ Amigen (according to our analysis contains 30 mEq. of sodium, 19 mEq. of potassium, 21 mEq. of chloride and 6.11 gm. of nitrogen per liter) furnished by Mead Johnson & Company, Evansville, Ind.

§ Travamin (5% travamin solution contains, according to our analysis, 112 mEq. of sodium, 54 mEq. of chloride, 4.9 mEq. of potassium, and 6.13 gm. of nitrogen per liter, and the 6% solution contains 140 mEq. of sodium, 58.8 mEq. of chloride, 6.25 mEq. of potassium, and 6.9 gm. of nitrogen per liter) supplied by Baxter Laboratories, Inc., Morton Grove, Ill.

tained for the following three days on 3 liters of fructose in water, with 1 liter of 6% plasma hydrolysates in 12 per cent invert sugar and additional electrolytes. On Nov. 22, one-fourth of his caloric and chemical intake was provided by oral diet and the remainder with intravenous fluids. On Nov. 25, one-half of the caloric and chemical constituents of this diet was made up with oral intake and the remaining half with intravenous intake. On Nov. 29, the patient received a full diet which was equal with respect to calories and chemical constituents to his original I. V. regimen. Prior to his discharge on Dec. 2, 1953, the patient exhibited a sustained weight gain, with good appetite and general improvement.

W. B. (U. H. C. 157-238), a 61-year-old white man was admitted to the Medical Service on Nov. 10, 1953. Roentgenograms showed marked retention of fluid and food particles although some administered barium passed through the pylorus and down the gastrointestional tract. An ulcer crater was demonstrated on the lesser curvature of the stomach, near the pylorus. The patient was transferred to the Surgical Metabolic Division on Nov. 12, 1953, and was given 2,000 cc. of 5% protein hydrolysates in 10% fructose. The following day he received 1,000 cc. of 5% protein hydrolysates in 10% fructose, 1,000 cc. of 6% plasma hydrolysates in 12% invert sugar, and 400 cc. of 10% fructose. He was also given 600 cc. of intravenous fat (Lipomul I. V.) and parenteral vitamins, and potassium chloride was added to provide a daily intake of 100 mEq. The following day he received 1,000 cc. of 5% protein hydrolysates in 10% fructose and 1,000 cc. of 6% plasma hydrolysates in 12% invert sugar, and 1,600 cc. of 10% fructose along with 600 cc. of Lipomul intravenously. For the next five days the patient received daily 1,000 cc. of 5% protein hydrolysates in 10% fructose, 1,000 cc. of 6% plasma hydrolysates in 12% invert sugar, and 1,000 cc. of 10 % fructose solution, and 600 cc. of intravenous fat solution. At the end of this time, the patient was started on an oral diet which he tolerated fairly well. He was given 500 cc. of blood on Nov. 19, 22, and 23. On Nov. 27, the patient was taken to surgery and a hemigastrectomy-vagotomy with a Billroth-I type anastomosis was done. The day of operation he received 3,000 cc. of 10% fructose solution and 950 cc. of whole blood. On the first and second postoperative days he was given 3,000 cc. of 10% fructose daily and 600 cc. of intravenous fat solution. On the third and fourth postoperative days, the patient was given 1,000 cc. of 10% fructose, 600 cc. of intravenous fat and 2,000 cc. of 5% protein hydrolysates in 10% fructose. On the fifth postoperative day 1 liter of protein hydrolysates was omitted from the above regimen, and the patient was started on an equal amount of calories and chemical constituents by mouth. This was continued through Dec. 2, 3, and 4, and on Dec. 5, the intravenous solutions were changed to 1,000 cc. of 5% protein hydrolysates in 10% fructose and 600 cc. of intravenous fat, while alimentary supplements were utilized to provide the caloric and chemical equivalents of the previous regimen. This was carried out through Dec. 5, 6, 7, and 8. On Dec. 9, the patient was given a completely oral regimen. His prestudy weight was 42 kg. A sustained daily caloric intake of 2,500 Cal. during this period, which included the day of surgery, was accompanied by no significant weight loss.

J. S. (U. H. C. 199-144), a 61-year-old white man, was admitted to the Medical Service on Oct. 8, 1953, with a known diagnosis of peptic ulcer. He had proved duodenal ulcer in 1939 and a proved gastric ulcer in 1944. He began having increasing epigastric distress a month prior to admission, and one week before returning to the hospital he began having severe epigastric pain, nausea, and frequent vomiting. He noted that the symptoms were severer when lying down. Roentgenograms taken on Oct. 12 revealed a hiatus hernia, and a marked deformity of the duodenal bulb due to an ulcer crater in this region. Repeat roentgenographic studies on Nov. 17, showed dilatation of the stomach, with a significant degree of gastric retention which prevailed after three hours. The patient was transferred to the Metabolic Division on Oct. 31 and balance studies were started, which continued through Nov. 3, during which time a constant diet was maintained. On Nov. 4 he was taken to surgery and a hemigastrectomy-vagotomy was done with a Billroth-I type anastomosis. Postoperative roentgenographic studies on Nov. 18, 1953, revealed a delayed emptying of the stomach and a delay in the transit time of ingested barium through the small bowel. There were no symptoms and the patient was discharged much improved.

F. U. (U. H. C. 652-244), a 49-year-old white man, was admitted on Oct. 24, 1953, because of persistent vomiting and marked weight loss. He had had frequent vomiting after eating and severe heartburn for the past five to eight years. Roentgenograms at the time of admission

revealed two gastric ulcers and pyloric obstruction. In addition, the patient had lost 20 lb. (9 kg.) in the previous six months. He was transferred to the Surgical Metabolic Division on Oct. 25, the day following admission, and was given an intravenous regimen, with nothing by mouth. He received 600 cc. of intravenous fat, 1,000 cc. of 5% protein hydrolysates in 10% fructose, 1,000 cc. of 6% plasma hydrolysates in 12% invert sugar, and 1,000 cc. of 10% fructose with potassium added to make a total intake of 100 mEq. per day. He was placed on continuous gastric suction which yielded daily amounts of drainage ranging from 600 to 1,500 cc. On Oct. 30, a liquid oral regimen was started, with an intake comparable, chemically and nutritionally, to the intravenous intake, which he had received on the previous five days. Gastric analysis showed large amounts of free hydrochloric acid following histamine and insulin. On Nov. 5, the patient was taken to surgery and a hemigastrectomy-vagotomy with a Billroth-I type of anastomosis was performed. Postoperatively, the patient continued to be given an intravenous regimen for the first four days. He received 1,000 cc. of whole blood and 3,000 cc. of 10% fructose on the day of operation. On the following three days 3,000 cc. of 10% fructose were given. On the fifth and sixth postoperative days he received 1,000 cc. of 10% fructose and 2,000 cc. of 5% protein hydrolysates in 10% fructose, with sufficient potassium added to equal 100 mEg. per day. Thereafter, the caloric and chemical equivalent of his preoperative regimen was given orally, and the patient was discharged greatly improved on Nov. 21, 1953.

S. A. (U. H. C. 636-575), a 57-year-old white woman, was admitted to the Metabolic Ward at 3:50 p. m. on Jan. 12, 1953, because of pyloric obstruction following stenosis of a chronic peptic ulcer. She had lost considerable weight, was markedly malnourished, and had been urged to come into the hospital on many previous occasions. She was an extremely nervous woman who had had many complaints and preconceived ideas. She had lost about 50 lb. (23 kg.) in the 10 months since the onset of her present illness. She had been admitted to the hospital the latter part of October, 1952, because of symptoms of pyloric obstruction, but before adequate studies could be carried out and treatment instituted she left the hospital against advice. The roentgenograms taken prior to October, 1952, had shown almost complete pyloric obstruction; however, owing to the large amount of retained fluid, adequate films were not obtained. Roentgenograms taken on Jan. 20, 1953, showed a marked degree of pyloric stenosis with no evidence of tumor, and it was thought that the obstruction was secondary to a peptic ulcer. The patient was extremely apprehensive and refused to consider surgery. Studies were undertaken in the hope of proving to the patient that she was unable to eat. This case afforded an unusual opportunity to observe the changes in a patient eating a liquid diet low in potassium while on gastric suction and to observe the serum electrolyte and metabolic alterations which would result. By observing the patient and making blood chemical determinations and taking electrocardiograms as indicated it was felt that no serious complications would occur which could not be readily corrected by proper parenteral therapy. After three days, the patient had lost almost everything taken by mouth through intermittent gastric suction. Her serum sodium concentration, prior to the onset of the study, had been 144 mEq. per liter and fell to 135 mEq. per liter. Serum chloride concentration decreased from 98 to 84 mEq. per liter, CO_2 went from 80 to 101 vol.%, serum potassium concentration fell to 2.9 mEq. per liter, and blood pH rose from 7.35 to 7.53, while the hematocrit of 35 increased to 44. After becoming quite weak and tired, the patient agreed to a parenteral regimen. For two days she was given 2,000 ml. of 5% dextrose in isotonic sodium chloride and 1,000 ml. of 5% dextrose in water. An EKG taken at this time showed changes consistent with hypokalemia; 80 mEq. of potassium were given intravenously in 5% dextrose in water. She subsequently felt much improved and her electrocardiogram was interpreted as normal. The administration of saline and potassium chloride was followed by a decrease in the hematocrit to 33 and blood pH to 7.40, coincident with a rise in sodium concentration to 143 mEq., the serum chloride to 110 mEq., and the serum potassium to 4.2 mEq. per liter. The volume of gastric fluid drainage decreased markedly when little or nothing was permitted by mouth. After this, the patient was given 5% protein hydrolysates in 5% dextrose with added potassium. Her improvement was so pronounced after two days that she insisted on leaving the hospital unless she was allowed to eat. Unfortunately, studies were discontinued at this point because it was believed that she would never cooperate. After eating fairly well for two and one-third days she felt nauseated and vomited 1,150 ml. A gastric tube was reinserted and parenteral fluids given. She lost an additional 5,270 ml. of gastric drainage over the next 40 hours. After extensive

parenteral preparation a hemigastrectomy and vagotomy were done on Jan. 27, 1953. Her postoperative course was entirely uneventful, and she gained 6½ lb. (3 kg.) over her first seven postoperative days.

D. B. (U. H. C. 635-404), a 42-year-old white man was admitted to the hospital on Sept. 23, 1952, because of severe pain in the epigastrium of two weeks' duration. Tarry bowel movements had also been noted during this period. He had had two similar attacks in the past, the first being four years prior to this hospital admission, while he was in the Ohio State Penitentiary, and the second occurring two years ago, when he was admitted to another hospital where a diagnosis of peptic ulceration was made. The patient had lost 17 lb. (8 kg.) in the two weeks prior to admission. Physical examination was not remarkable, except for a diffuse abdominal tenderness, most marked in the upper abdomen. On Sept. 26, 1952, roentgenograms revealed an almost complete obstruction of the pylorus probably due to ulcer, but carcinoma could not be excluded. He was transferred to the Surgical Metabolic Division on Sept. 25, 1952, where he received intravenously 1,500 ml. of 5% dextrose in isotonic sodium chloride and 2 liters of 5% plasma hydrolysates in 5% dextrose. The two days prior to transfer to the Metabolic Division he had received 2 liters of 5% dextrose in water and 2 liters of 5% dextrose in isotonic sodium chloride on the first day, and 2,000 cc. of 5% dextrose in water and 3,000 cc. of 5% dextrose in isotonic sodium chloride on the second day. Starting on Sept. 26, and for the next six days, the patient received 1,000 cc. of 5% dextrose in water, 1,000 cc. of 5% dextrose in isotonic sodium chloride, and 2,000 cc. of 5% plasma hydrolysates in 5% dextrose solution, with 50 to 100 mEq. of potassium chloride added. His balance studies began four days prior to surgery. The same parenteral fluid regimen was continued until the day of operation, at which time he received 1,500 cc. of whole blood, 200 cc. of 5% dextrose in water, 2,000 cc. of 10% fructose in water, and 400 cc. of isotonic sodium chloride. On Oct. 2, 1952, exploration was performed, and a gastroenterostomy and vagotomy were done. Thereafter, he was maintained on 10% fructose solution for seven days, until Oct. 9, at which time he was given 2,700 cc. of 10% fructose and started on fluids by mouth. The patient's weight on admission to the Metabolic Division was 60.3 kg., and it fell to a low of 51.7 kg. on his ninth postoperative day, and thereafter increased somewhat, reaching 53.9 kg. at the time of discharge on Oct. 15.

M. K. (U. H. C. 638-407), a 43-year-old Negro woman, was admitted to the Metabolic Division on Dec. 3, 1952, with a history of vomiting and cramping abdominal pain of 24 hours' duration. In April, 1952, the patient had been operated upon for a penetrating gunshot wound of the abdomen. The patient's temperature at the time of this admission was 38.2 C., and the blood pressure was 155/115. She was admitted directly to the Surgical Metabolic Division, where fluid therapy was given. On Dec. 4, an exploratory laparotomy was performed which revealed a closed-loop obstruction of the ileum due to adhesions. Lysis of the adhesions was performed with relief of the intestinal obstruction. On the day of admission, the patient received 2,000 cc. of 5% dextrose in water and 3,000 cc. of 5% dextrose in saline (1,000 Cal.). The following day she received 4,000 cc. of dextrose in water, 500 cc. of whole blood, and 500 cc. of isotonic sodium chloride (800 Cal.). The next four days she received 1,000 cc. of 5% dextrose in water and 2,000 cc. of 5% plasma hydrolysates in 5% dextrose (1,000 Cal.), with parenteral vitamins added. Her temperature, which had fallen to normal after adequate hydration, rose to 39 C. the day after surgery, and gradually subsided over the following nine days. The hematocrit reading was 43 at the time of admission, and after hydration it fell to 37. It was 39 on the day after surgery and continued to rise to 41 on Dec. 8, where it remained until the time of discharge. Serum chlorides were 100 mEq. per liter on admission, fell to 94 mEq., and gradually rose to 103 mEq. per liter on Dec. 12. Serum sodium was 144 mEq on the day of admission, fell to 136 mEq. postoperatively, and gradually rose to 140 mEq. on Dec. 12. Serum potassium initially was 4.8, fell to a low of 4.1 on Dec. 12, and remained in this normal range until discharge on Dec. 15, 1952.

A. W. (U. H. C. 202-627), a 63-year-old Negro, was first admitted to this hospital on Jan 29, 1940, for a myocardial infarction. Forty-eight hours prior to the present admission, the patient was seized with cramping lower abdominal pain, which radiated to the epigastrium and persisted intermittently until the time of admission. He had had no previous gastrointestinal disturbances. His blood pressure at the time of admission, at 7:45 p. m. on Sept. 30, 1952, was 160/110; pulse rate 98; temperature 38 C, and respiration rate 18. There was a somewhat

generalized purplish mottling of the skin. His finger beds appeared cyanotic, and there were a few inspiratory and expiratory wheezes in the chest. The abdomen did not appear to be distended. The liver margin was felt 2 fingerbreadths below the costal margin and was moderately tender. Roentgenograms on admission showed an abnormal intestinal gas pattern which was consistent with small bowel obstruction. Exploratory laparotomy was performed 18 hours after admission, and a volvulus of the small intestine was reduced, after which a defect in the mesentery was sutured. The patient tolerated the procedure fairly well. He was given nothing by mouth until the third postoperative day when he was allowed small sips of water. On the day of admission he received 1,100 cc. of 5% dextrose in water and 1,000 cc. of 5% dextrose in isotonic sodium chloride, and 500 cc. of whole blood. The following day he received 3,000 cc. of 5% dextrose in water. The next day 2,300 cc. of 5% dextrose in water and 700 cc. of 5% dextrose in saline were given. The next three days he received 3 liters of 5% dextrose in water. His postoperative course was complicated by a wound infection, which was first recognized on Oct. 6, 1952. Drainage of the wound was followed by prompt healing.

W. G. (U. H. C. 645-126), a 31-year-old Negro, was admitted to the University Hospitals of Cleveland on May 9, 1953, complaining of vomiting and cramping abdominal pain of 12 hours' duration. At the time of admission to the Emergency Ward his temperature, pulse rate, respiration, and blood pressure were within normal limits. Hemoglobin content was 14.5 gm. per 100 cc., white blood cell count 8,000; urine examination was negative, with a specific gravity of 1.027. In April, 1952, the patient was stabbed in the left upper abdomen. This necessitated an abdominal exploration at another hospital. Abdominal examination at the time of this admission revealed a healed left rectus incision, abdominal tenderness, distention, and hyperactive bowel sounds, especially in the left lower quadrant. Roentgenograms taken shortly after admission were not remarkable, but a clinical diagnosis of intestinal obstruction was made. After adequate intravenous hydration the patient was taken to surgery where an obstruction of the ileum was released after lysis of adhesions. The patient received 600 cc. of 5% dextrose in water, 600 cc. of 5% dextrose in saline, 500 cc. of isotonic sodium chloride, and 2,000 cc. of 6% plasma hydrolysates in 12% invert sugar on the day of admission. For the next three days, he received 2,000 cc. of 6% plasma hydrolysates in 12% invert sugar, except on the third day when he was given 1,000 cc. of 5% plasma hydrolysates in 10% invert sugar in place of 1,000 cc. of 6% plasma hydrolysates in 12% invert sugar. In addition, he was given 1,000 cc. of 10% invert sugar daily. On the fifth hospital day, he was given 2,000 cc. of 5% plasma hydrolysates in 10% invert sugar and 500 cc. of 10% invert sugar in water. On the sixth and seventh hospital days he received 2,000 cc. of 5% plasma hydrolysates in 10% invert sugar and 1,000 cc. of 10% invert sugar in water. On the eighth hospital day, the regimen was changed to include 2,000 cc. of 5% protein hydrolysates in 5% dextrose and 1,000 cc. of 10% invert sugar in water, and this was continued for a three-day period at which time the studies were terminated. In addition to the amount contained in the intravenous plasma hydrolysates, the patient received potassium chloride, 90 mEq. a day on the first four days, and 50 mEq. a day on the next four days. The serum chlorides on May 11 were 104; on May 13, 102, and May 15, 101. Serum sodium was 136 on May 11 and 143 on May 13; serum potassium was 4 on May 11, 4.2 on May 3, and 4.2 on May 15. The CO_2-combining power on four occasions ranged from 63 to 69 Vol.%.

P. J. (U. H. C. 141-578), a 52-year-old Negro woman, was admitted to the hospital on March 13, 1953, with a complaint of cramping abdominal pain. A diagnosis of partial obstruction of the small intestine was made, and a long intestinal tube was inserted. The patient had been in this hospital three months previously because of intestinal obstruction, at which time a lysis of adhesions was performed. The day of admission she received 670 ml. of 5% dextrose in water and 1,000 ml. of 5% dextrose in isotonic sodium chloride solution. On each of the next three days she received 1,000 ml. of 10% dextrose in water and 2,000 ml. of 5% plasma hydrolysates in 10% invert sugar, and 65 mEq. of potassium chloride intravenously. A liquid diet was started on the fourth hospital day and continued until the time of operation, on March 24, the 11th hospital day. Exploratory laparotomy performed at this time revealed a scirrhous carcinoma of the stomach with widespread peritoneal metastasis. She was given 1,800 ml. of 5% dextrose in isotonic sodium chloride and 500 ml. of whole blood on the day of operation. Intravenous fluids for the next three days consisted of 1,000 ml. of 10% dextrose in water and 2,000 ml. of

5% plasma hydrolysates in 10% invert sugar. An oral diet was started on the fourth postoperative day and maintained until the time of discharge on April 9, 1953. Her admission weight was 41.7 kg., and her weight at the time of discharge was 43.3 kg.

W. S. (U. H. C. 631-608), a 32-year-old, well-developed, and well-nourished Negro man, was admitted with a three-hour history of abdominal pain, nausea, and vomiting. The last normal bowel movement occurred three days prior to admission. Findings on admission were as follows: temperature, 37.2 C; pulse rate, 84; respiration rate, 32, and blood pressure 140/84. The abdomen was distended, tympanitic with hypoactive bowel sounds. Roentgenogram revealed a distended small bowel pattern consistent with mechanical intestinal obstruction. Ten hours after admission, the patient was taken to surgery, where a volvulus of the small intestine was reduced and a Meckel diverticulum and 8 in. (20 cm.) of small intestine were resected. About 300 to 400 ml. of serosanguineous fluid was removed from the peritoneal cavity, and approximately 3,500 ml. of fluid and considerable gas were aspirated from the small intestine to decompress it so that the resection could be performed. He received 1,000 ml. of whole blood during the operation. On the day of operation, the patient was given 1,500 ml. of 5% dextrose in saline, 1,000 ml. of isotonic sodium chloride solution, 2,000 ml. of 5% dextrose in water, and 2,000 ml. of 5% plasma hydrolysates in 5% dextrose (this latter solution contains approximately 112 mEq. of sodium, 4.9 mEq. of potassium, and 55 mEq. of chloride per liter). The first eight postoperative days the patient received a daily intravenous infusion of 2,000 ml. of 5% plasma hydrolysates in 5% dextrose and 1,000 ml. of 10% dextrose in water. On the seventh and eighth postoperative days a large amount of potassium was given. The immediate postoperative period was complicated by a temporary oliguria, hypotension, tachycardia, and, subsequently, by a delay in the restoration of normal intestinal activity.

W. M. (U. H. C. 633-130), a 68-year-old Negro man, had been discharged from University Hospitals on Aug. 12, 1952, following a right inguinal herniorrhaphy for incarcerated hernia. The patient developed cramping abdominal pain on Aug. 15, which became increasingly severe and resulted in his readmission to University Hospitals on this date. Physical examination at this time revealed a well-developed, poorly-nourished, dehydrated, elderly man, who appeared to be in acute distress. His abdomen was distended, diffusely tender, and without visible peristalsis. The abdomen was tympanitic, and bowel sounds were hyperactive. Roentgenograms of the abdomen were consistent with mechanical obstruction of the small intestine. The patient was given intravenous fluids, and a long intestinal tube was passed. He was taken to surgery four hours later, where relief of an obstruction of the ileum was accomplished with the use of spinal anesthesia. It was necessary to resect approximately 25 cm. of the ileum, and an ileoileostomy was performed. From the time of admission until 6:30 a. m. the following morning, the patient received 2,400 cc. of 5% dextrose in water, 2,000 cc. of 5% dextrose in saline, 500 cc. of whole blood, and 100 cc. of isotonic sodium chloride solution. Blood chemistries the morning after surgery revealed a chloride of 80 mEq. per liter, CO_2-combining power 55 mEq. per liter, and BUN 18 mg. per 100 ml. The patient received 2,000 cc. of 10% dextrose in water and 1,400 cc. of 5% plasma hydrolysates in 5% dextrose for the first four postoperative days. On his fifth postoperative day, he received a liquid diet which was supplemented by intravenous therapy of 390 ml. of 10% dextrose in water and 650 ml. of 5% plasma hydrolysates in 5% dextrose. The next two days he was given 2,000 ml. of 10% dextrose in water and 1,400 ml. of 5% plasma hydrolysates in 5% dextrose after which he was given a complete oral regimen and did very well until discharge from the hospital on Aug. 30, 1952.

S. M. (U. H. C. 654-186), a 55-year-old white man, was admitted to the Metabolic Service because of weight loss, epigastric cramping pain, and marked abdominal distention. Except for some mild symptoms, the patient had been fairly well until three weeks prior to his admission to the hospital, when he began to have abdominal distress. He had lost 8 to 10 lb. (3.6 to 4.5 kg.) in the previous six weeks. The patient had had acute appendicitis at the age of 16 years, and two weeks after an appendectomy, he developed an acute intestinal obstruction which was treated by surgical intervention. On this admission, the patient's temperature, pulse rate, respiration, and blood pressure were within normal limits. He was a well-developed, well-nourished, white man, in no acute distress; however, there was evidence of marked intestinal distention. Roentgenograms of the abdomen, taken shortly after admission, showed large dilated loops of bowel, which were interpreted as large bowel. Barium enema done at this time showed the barium to

pass freely through the rectum and sigmoid colon up to the splenic flexure and then promptly empty into large fluid and air-filled loops which occupied almost the entire abdominal cavity. No definite diagnosis could be made at this time. A long intestinal tube was inserted, and its progression was followed by subsequent roentgenograms. Twenty-four hours later it had entered the jejunum. Subsequently, it advanced down to the terminal ileum. The patient was given an intravenous regimen with nothing by mouth and received 2,000 ml. of 5% protein hydrolysates in 10% fructose on the day of admission. The following four days he received 2,000 cc. of 5% protein hydrolysates in 10% fructose and 1,000 cc. of 6% plasma hydrolysates in 12% invert sugar. This intake varied only on the first day of therapy, when only 700 cc. of 6% plasma hydrolysates in 12% invert sugar was given. By the sixth day the patient was much improved, and oral feedings were begun, and the long tube which had reached the terminal ileum was removed. The patient felt so well at this time that he refused operation and was subsequently discharged from the hospital on Dec. 19, 1953.

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MASSIVE GASTROINTESTINAL BLEEDING

Study of Two Hundred Ninety-Six Patients at City Hospital of Cleveland

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MASSIVE gastrointestinal bleeding causes dramatic signs and symptoms for the patient and presents a challenge to the internist, the surgeon, and the radiologist. The source of such bleeding often remains obscure to the very end, and the mortality is high. A review of available data from several centers shows considerable variation in the incidence of massive bleeding, in the source of the bleeding, and in the mortality resulting from it. In order to obtain information bearing on these variables, the records of patients admitted to City Hospital of Cleveland because of gastrointestinal bleeding between the years 1941 and 1951 inclusive were reviewed and analyzed.

DEFINITION

As emphasized by the work of Stewart [1] and his associates, interpretation of data concerning massive gastrointestinal hemorrhage must be qualified by a definition of the term. Welch [2] showed, for instance, that by taking a red blood cell count of 2,500,000 per cubic millimeter of blood instead of 3,000,000 per cubic millimeter, the mortality was raised from 8.0 to 13.0%.

The patients studied for this report were classified on the basis of clinical evaluation alone. Stewart [1] defined massive gastrointestinal hemorrhage as that resulting in a diminution of the circulating blood volume to 60% or less of the normal. While this criterion does not take into account the fact that similar blood-volume deficits may have different effects in different persons, it nevertheless provides a useful point of reference. During the period of this study, however, methods for determination of the circulating blood volume were not available to this hospital. In the belief that careful appraisal of the clinical findings can serve as a useful indication of the degree of blood loss, the following criteria were used for determining massive hemorrhage in this study:

1. Clinical evidence of hemorrhagic shock
2. Syncope related to hematemesis or melena of more than 1 liter (estimated)
3. Continued blood loss during the period of one week at no time sufficient to cause syncope or shock but enough to cause a hematocrit reading below 25% and a hemoglobin concentration below 8 gm. per 100 cc.

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On the basis of these criteria, of 442 patients admitted to City Hospital of Cleveland between 1941 and 1951 because of gross bleeding into the gastrointestinal tract, 296 (or 67%) were classified in the group with massive gastrointestinal bleeding. This experience is comparable to that reported by Sandusky and Mayo [3] but is higher than that reported from other clinics.* Twenty per cent of the patients in this report had red blood cell counts of between 3,000,000 and 5,100,000 per cubic millimeter of blood and hemoglobin concentrations of 10 to 17.0 gm. per 100 cc. They were nevertheless considered to have had massive hemorrhage by the criteria outlined above.

SOURCE OF BLEEDING

Table 1 shows the incidence of the various causes for massive gastrointestinal tract bleeding in this group of 296 patients. It will be noted that nearly half of the patients bled from benign ulcers of either the duodenum (35% of the total number of cases) or the stomach (12% of the total). A high proportion of this group bled massively from esophageal varices (23%), which accounts in part for the high mortality in this series of cases. Seven patients (2%) bled massively

TABLE 1.—*Sources of Massive Gastrointestinal Bleeding Reported by Various Authors*

	Stewart [22]		Gott and Smith [23]		Welch [2]		Costello [24]		Warthin and Warren [25]		City Hospital of Cleveland	
Source	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Duodenal ulcer	60	48.3	114	58.6	210	59	171	57.0	48	55.8	103	35.0
Gastric ulcer	46	37.0	19	9.7	41	11	33	11.0	7	8.1	35	11.6
Gastrojejunal ulcer	4	3.2	3	1.5	8	2	4	1.3	1	1.0	3	1.0
Esophageal varices	3	2.4	1	0.5	62	17	24	8.0	8	9.3	68	23.0
Miscellaneous	9	7.3	11	5.6	35	9	64	21.3	8	9.3	25	8.4
Undetermined	1	1.0	47	24.1	8	2	4	1.3	14	16.3	62	21.0
Total	123	100	195	100	364	100	300	100	86	100	296	100
Over-all mortality, %		11.2		5.6		25		25		12.8		40

from malignant lesions (five of the stomach, one of the esophagus, and one of metastatic squamous-cell carcinoma of the gastrointestinal tract). One patient bled massively from a benign polyp of the sigmoid and one from a leiomyoma of the stomach. In one-fifth of the patients who were admitted to the hospital for massive gastrointestinal-tract bleeding, the source of the bleeding remained undiagnosed. This compares with the figures of 1 to 24.1% of the total cases reported in the literature (Table 1).

SEX AND RACE IN MASSIVE GASTROINTESTINAL BLEEDING

Table 2 shows the expected preponderance of massive gastrointestinal hemorrhage in the male (3.5:1). It also demonstrates, unexpectedly, the greater proportion of white than Negro men and women in this group of 296 patients. The over-all ratio of white to Negro patients was 5:1. The ratio of whites to Negroes in the general patient population of this hospital is 4:3. Review of the available literature † provides no clear-cut evidence that the incidence of peptic ulcer differs between whites and Negroes.

* References 4 and 5.

† References 6 to 9.

DIAGNOSIS OF SOURCE OF BLEEDING

Rational and direct therapy of massive gastrointestinal-tract bleeding depends upon precise localization of the source of bleeding. Published reports (Table 1) show considerable variation in the proportion of patients with massive bleeding for whom the source of the hemorrhage remains undiagnosed.

The history, present and past, when obtainable, provided useful information in this group of patients. The history of ulcer ‡ in the past or of alcoholism and ascites was seldom misleading when obtainable, especially when the history of the latter was supported by specific findings at physical examination (hepatosplenomegaly, ascites, spider angiomata) and by laboratory tests (evidences of deranged liver function). Anticipating surgical therapy, however, the surgeon so far as possible needs to have more concrete evidence with regard to localization of the source of

TABLE 2.—*Race and Sex Incidence in Massive Gastrointestinal Bleeding*

	Patients					
		Females			Negro	
Etiology	Males, No.	No.	%	White, No.	No.	%
Duodenal ulcer	76	27	26.2	77	26	25.2
Gastric ulcer	26	9	26.0	24	11	31.4
Esophageal varices	54	14	20.4	64	4	5.8
Miscellaneous	22	6	21.4	27	1 *	3.6
Undetermined	53	9	14.5	57	4	6.4
Total	231	65	22.0	249	47	15.8

Ratio: Male to female = 3.5:1; white to Negro = 5:1

* Negro woman with carcinoma of stomach and massive bleeding.

TABLE 3.—*Evidence for Source of Massive Gastrointestinal Bleeding*

Source	Clinical Alone	X-Ray	Endoscopy	Operation	Autopsy	Combined
Duodenal ulcer	15 *	89	..	20	4	103
Gastric ulcer	..	24	6	15	6	35
Esophageal varices	28 †	19	5	9	18	68
Total ‡	43	132	11	44	28	206

* In this group clinical evidence is as follows: "typical" ulcer history, history of perforation, previous x-ray examination in other hospital, etc.

† In this group clinical evidence is as follows: chronic alcoholism, hepatosplenomegaly, spider angiomata, ascites, deranged liver function tests, and liver biopsy.

‡ Those bleeding from miscellaneous sources are omitted.

bleeding than can be obtained by clinical history and physical examination alone. He would at least want to know whether the bleeding stems from the esophagus above the diaphragm or from the stomach and intestine below the diaphragm.

To aid the clinical impression gained from the history and physical examination, x-ray study of the upper gastrointestinal tract was done at this admission in 199 of the 296 cases and endoscopy was done in 17. Positive roentgenologic diagnoses were made in 150 cases. Esophagoscopy or gastroscopy led to a positive diagnosis in 11 cases. This experience is summarized in Table 3. The examinations were done as emergency procedures in 60% of the cases during the period, July, 1948, to

‡ Only 34% of the 296 cases had a previous history of ulcer, and 19% had a history of previous bleeding.

December, 1949, as reported by Elmer and Rousuck.[10] It is noteworthy that 21 of the 62 patients whose conditions remained undiagnosed died without operation during the first 48 hours after the onset of bleeding.

The relatively low proportion of cases with bleeding from gastroduodenal ulcer (47% of the 296 cases) is at variance with the experience of other clinics (Table 1) and is attributable to the high incidence of bleeding from esophageal varices in the cases described in this report. In a large number of the cases in which the source of bleeding was undetermined, the patients may have bled from gastroduodenal ulcers.

TREATMENT IN THIS GROUP OF 296 CASES

Only 50 patients were treated by operation (Table 4). Of these, 30 who were bleeding from benign ulcer of the stomach or duodenum were treated by gastric resection (with the exception of 1 out of 19 patients with duodenal ulcer for whom vagectomy was done and 1 out of 11 with gastric ulcer for whom gastrotomy and ligature of the bleeding point was done).

TABLE 4.—*Relative Incidence of Operative and Nonoperative Mortality in Cases with Massive Gastrointestinal Bleeding of Different Etiologies*

	Total Cases			Cases Treated Medically			Cases Treated Surgically		
Source	Cases, No.	Deaths, No.	Mortality, %	Cases, No.	Deaths, No.	Mortality, %	Cases, No.	Deaths, No.	Mortality, %
Duodenal ulcer	103	15	14.5	84	10	12	19	5	26
Gastric ulcer	35	11	31	24	8	33	11	3	27
Gastritis	5	0	0	5	0	0	0	0	0
Esophageal varices	68	52	76.6	59	49	83	9	3	33
Miscellaneous	23	11	48	18	10	55	5	1	20
Undetermined	62	29	46.8	56	29	52	6	0	0
Total	296	118	40	246	106	43	50	12	24

Of the nine patients who had bleeding from esophageal varices and were treated surgically, three were treated only by injecting the varices with sclerosing solution (sodium morrhuate). Three others had subtotal gastrectomy (two cases) and portacaval shunt (one case) when injections failed. One case [11] had only exploratory laparotomy, a contemplated portacaval shunt was not done when it was observed that the portal pressure was normal. One of the nine cases had primary subtotal gastrectomy and one had primary portacaval anastomosis.

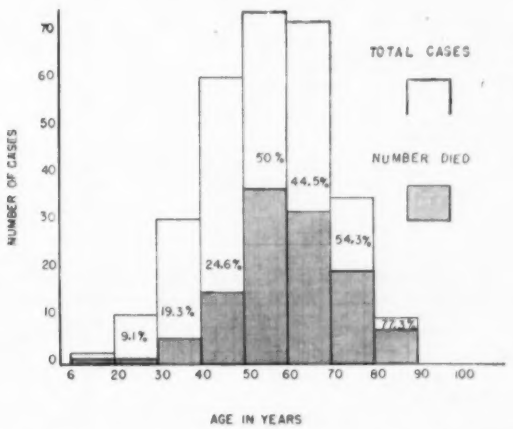
Five miscellaneous operations were done: two for carcinoma of the stomach, one for repair of diaphragmatic hernia, one for excision of leiomyoma of the stomach, and the fifth for excision of a sigmoidal polyp.

Of the six cases that had operations performed but in which no diagnosis of the source of bleeding could be made, subtotal gastrectomy was done in five; gastrotomy alone was done in one. Bleeding ceased in all of them.[12]

Medical treatment, consisting of transfusions of blood and other supportive measures, Meulengracht diet, antacids, antispasmodics, and sedatives, was carried out in 246 cases. Intraesophageal tamponade was done in five of the patients who were bleeding from esophageal varices.

HOSPITAL MORTALITY

Of the 296 patients admitted with massive gastrointestinal bleeding, 118 died, a mortality of 40%. If those treated by operation are excluded, 106 of the 246 died, a mortality of 43%. The surgical mortality was 24% (12 out of 50 cases). This mortality was lowest for the group who were operated upon for bleeding of undetermined source (Table 4). The differences in mortality for the other groups are of no statistical significance. When the 11-year period is divided into an early one, of six years, and a later one, of five years, it is found that the mortality rate for the medically treated cases remained unchanged (41% of 105 cases in the first period and 44% of 141 cases in the second period). There is an improvement, however, in the mortality rate for those treated surgically in the second period. During the first six-year period, 4 of 12 patients who were operated upon died; during the second period of five years, 8 of 38 patients died, a mortality of 33% for the first group and 21% for the second. Many factors must have contributed



Relationship of age to incidence and mortality in massive gastrointestinal hemorrhage.

to this improvement in the surgical mortality—technical improvements, greater availability of blood for transfusion, anesthesia, and the judicious use of antibiotic agents. The combined medical and surgical mortality was 41% for the first six years (117 cases) and 39.4% for the subsequent five years (179 cases).

Of the 118 patients who died, 38 died during the first 48 hours of hospital stay. None of these had surgical intervention except for two patients in whom the esophageal varices were injected with sclerosing solution. In a high proportion of these cases (21 of the 38), the bleeding remained undiagnosed.

The striking effect of age upon over-all mortality is illustrated by the Chart. Less than 25% of the patients under the age of 50 died, while more than 50% of those over the age of 50 died. Among the patients treated surgically this effect of age was not demonstrable, undoubtedly a statistical effect of small numbers.

The data in Table 5 emphasize the danger of nonoperative treatment for patients in the older age group. The age of 50 is taken categorically as the dividing line. The data demonstrate the poorer prognosis of medical treatment for those beyond

the age of 50 than for the younger group of patients. They show, too, that in the older age group the prognosis of surgical treatment is better than that of medical treatment. The reverse appears true for the younger group. The interrelationships of the data are not changed by the exclusion of patients who bled massively from esophageal varices from the total group. The figures may be confounded, however, by the inclusion in the medically treated group of those patients with undetermined or miscellaneous diagnoses, most of whom were treated medically and had a high mortality. The number of such patients who may have bled from gastroduodenal ulcer, of course, is not known.

TABLE 5.—*Mortality Following Treatment of Patients with Massive Gastrointestinal Bleeding*

	Total No. of Patients		Lived		Died			
					Treated Medically		Treated Surgically	
	Treated Medically, No.	Treated Surgically, No.	Treated Medically, No.	Treated Surgically, No.	No.	%	No.	%
All patients beyond age of 50 yr....	155	36	67	29	88	56	7	20
All patients under age of 50 yr....	91	14	73	9	18	20	5	35
Patients with massive hemorrhage from esophageal varices								
Beyond age of 50 yr.....	46	6	4	4	42	91	2	33
Under age of 50 yr.....	13	3	6	2	7	54	1	33
All cases exclusive of esophageal varices								
Beyond age of 50 yr.....	109	30	63	25	46	42	5	17
Under age of 50 yr.....	78	11	67	7	11	14	4	36

TABLE 6.—*Causes of Death After Massive Gastrointestinal Bleeding*

Primary Causes	Total Cases, No.	Treated Medically	Treated Surgically
Hemorrhage * and shock.....	99	95	4
Pneumonia (aspiration)	2	2	..
Pulmonary edema	1	1	..
Pulmonary embolism	1	1	..
Coronary occlusion	1	1	..
Peritonitis	5	3	2
Postoperative bleeding	4	..	4
Hepatic failure (coma).....	2	1	1
Uremia	2	1	1
Tracheoesophageal fistula (carcinoma of esophagus).....	1	1	..
Total	118	106	12

* Additional causes associated with hemorrhage were bronchopneumonia in nine cases, coronary occlusion in one case, and uremia in two cases.

CAUSES OF DEATH

As one might expect, the leading cause of death was of hemorrhagic shock (Table 6). This was considered responsible for death in 99 of the 118 cases. In addition, 9 of the 99 cases proved to have bronchopneumonia and two had uremia. Of the five patients who died with peritonitis, two had perforated ulcer along with the massive bleeding; two developed postoperative subphrenic abscess, and one who died of massive bleeding from esophageal varices proved to have peritonitis from an unsuspected perforation of a gangrenous appendix. The two cases of perforated ulcer and the one case of perforated appendix had not been operated upon.

FOLLOW-UP HISTORY

Of the 296 patients admitted for massive gastrointestinal hemorrhage, 178 survived this episode of bleeding. The history of these patients after they left the hospital is illustrated in Table 7. It will be noted that 29 were lost to follow-up and 33 died. None of the 29 lost to follow-up was a surgical case, and of the 33 that died after leaving the hospital, 5 had been treated by operation.

Among those that had been treated without operation, five had recurrences of minor bleeding, which did not cause them to be hospitalized; four were hospitalized again for minor gastrointestinal bleeding, and four had gastric resection at other hospitals. Three patients who had been treated conservatively for massive bleeding from esophageal varices were readmitted to the hospital, and portacaval shunts were performed. One of these three died two years after surgery; the other two are living and well two to four years after operation.

Of the 38 patients who had been operated upon and survived, 5 were found to have died 1 to 10 years later. One (gastrectomy for bleeding duodenal ulcer) died

TABLE 7.—*Subsequent History of 178 Patients Who Had Massive Gastrointestinal Bleeding and Were Discharged*

	Total	After Medical Treatment	After Surgical Treatment
Living and well to end of 1952 without further treatment	100	67	33
Living, but have had minor bleeding requiring no hospitalization	5	5	0
Hospitalization and medical treatment	4	4	0
Hospitalization and gastrectomy	4	4	0
Hospitalization and portacaval shunt	3	3	0
Died of recurrence of massive bleeding	5	5 *	1
Died of heart disease	4	4	0
Died of miscellaneous causes	6	3	3 †
Died of unknown causes	18	17	1
Lost to follow-up	29	29	0
Total	178	140	38

* One of these patients died after portacaval anastomosis had been done at another admission.
† Two of these three patients died of cerebrovascular accident.

of cerebrovascular accident 1 year after operation, and another died of unknown cause 10 years after surgery. One patient died of cerebrovascular accident two years after gastrectomy for bleeding gastric ulcer. One, who was treated with portacaval shunt initially, died of recurrent bleeding two years later. One died of carcinoma of the stomach in less than one year. The remainder are well, including one patient now living six years after injection of bleeding esophageal varices and another who had only exploratory laparotomy when he was found to have normal portal pressures.[11] He has not had recurrent hemorrhage.

COMMENT

The limitations of the usual clinical and laboratory methods for the evaluation of the degree of gastrointestinal bleeding are well known. Promptly after an exsaguinating hemorrhage a patient will be oligemic but may exhibit a normal hematocrit value, red blood cell count, and hemoglobin concentration. On the other hand, a patient may have repeatedly lost minute quantities of blood over a prolonged period of time and may be found to have a normal circulating blood volume. He

will have a very low hematocrit value, red blood cell count, and hemoglobin concentration. While the latter type of patient may have a serious reduction in the total circulating red blood cell mass, he will not have the same hemodynamic problems of the first type, and the prognosis can be expected to be different.

The objective determination of the deficit of circulating blood volume is without doubt the most reliable single piece of information with regard to the degree of blood loss. Although good methods for such determination have been available and have been simplified during the past 20 years, the techniques are still considered experimental in most hospitals. In fact, there is much to be said for the clinical evaluation used in this report. By assessing the clinical phenomena, the examiner can take into account the individual differences of response to hemorrhage, whether these be due to age or other features of the patient's general condition or to individual differences in neurocirculatory reactivity. After all, the important consideration in this problem is not so much the absolute volume of blood lost, but rather the effect that this has on the patient's bodily economy.

The data presented suggest that in a high proportion of cases the diagnosis of the source of bleeding remained obscure (21% of the 296 cases). It will be noted that in 21 of these 62 cases the patients died less than 48 hours after admission and were never in condition to permit investigation of the source of bleeding. In this group, the antecedent history was either noncontributory or unobtainable. Of the remaining 41 patients, 8 died 3 to 36 days after admission, and the diagnosis of the source of bleeding could not be ascertained despite employment of all available diagnostic methods. In 33 patients who survived this episode of bleeding, the source of hemorrhage remained obscure despite repeated examinations of the gastrointestinal tract.

Both the over-all and the surgical mortalities in this series are unduly high (Table 4). It should be emphasized that the cases collected during the 11-year period covered by this study were not under the care of a special group making a study of the problem. The experience is unselected. All patients were indigent, and it is generally agreed that the mortality in such a group, with all the related problems they present, is much higher than in a nonindigent group. The high mortality in this series of patients may further be attributed to the high incidence of bleeding from esophageal varices. Out of 68 such patients, 52 died, a mortality of 77%. Recent technical improvements § will surely lower the mortality from this cause of massive gastrointestinal bleeding. Examination of Tables 4 and 5 suggests that adoption of a policy of early surgical therapy in the older age group can result in improvement of the over-all mortality rate primarily by affecting the results in two groups of patients: those bleeding from esophageal varices and those for whom the source of bleeding is not discovered. It is in these groups especially that aggressive tactics must be employed for early diagnosis and for judicious early operative treatment.

It is noteworthy that of the 12 patients who died after surgery 10 had been operated upon more than four days after the onset of bleeding. Two had been operated upon within 48 hours of the time of bleeding, but these two were seriously ill patients whose surgery consisted of injecting the bleeding esophageal varices. If patients with bleeding esophageal varices are excluded, all of the seven patients

§ References 13 to 15.

operated upon during the first three days of hospital admission survived. In contrast to this low mortality among the surgically treated patients early after admission to the hospital, a high proportion of the deaths (38 out of 106) among those treated without operation occurred during the first 48 hours after admission. There is no obvious advantage in delaying surgery, then, once the indications for it are clear. Many others || have emphasized that one loses the "golden opportunity" if surgical intervention is delayed beyond 48 hours after the onset of massive gastrointestinal hemorrhage. Time should be taken, except possibly in dire emergencies, to perform the minimum diagnostic procedures which will provide some idea of the source of bleeding.¶ Except for this, patients beyond the physiologic age of 50 years who have had massive gastrointestinal bleeding, even if for the first time, should be treated surgically without undue delay in the absence of contraindications. The elderly patient with generalized arteriosclerosis suffers progressive damage by repeated episodes of hypotension. Those younger than the age of 50 should be treated nonoperatively unless hemorrhage continues or is repeated. Although the patients who bled massively from esophageal varices and were operated upon are too few in number to warrant conclusions on a statistical basis, they do not essentially contradict the policy as outlined above.

It can be argued with justification that the patient with massive gastrointestinal hemorrhage is an emergency until he is well enough to be released from the hospital. When indications for surgery exist, operation should be done early rather than late. Consequently, x-ray examination of the upper gastrointestinal tract and of the lower tract along with direct inspection of the esophagus, rectum, and sigmoid according to indications should be done at the first available time of night or day after the patient is out of shock. To be sure, the diagnostic value of such examinations is not the same as that of a formal investigation done at an elective time, but one never knows when the elderly patient who has had one massive hemorrhage will have another. Armed with information adequate for distinguishing bleeding from above or below the level of the diaphragm and from above or below the sigmoid, the surgeon is in a better position to manage the problem intelligently.

SUMMARY AND CONCLUSIONS

A review of 296 patients admitted to City Hospital of Cleveland between 1941 and 1951, inclusive, because of massive gastrointestinal bleeding is presented. Of these, 138 cases (47%) were secondary to benign ulcer of the duodenum or stomach, and 68 (23%) were secondary to esophageal varices.

In this series of cases, there was a preponderance of men to women (the ratio being 3.5 : 1) and of white to Negro patients (the ratio being 5 : 1). The white to Negro ratio in the general population of this hospital is 4 : 3.

The importance of both clinical and laboratory appraisal of the severity of bleeding is emphasized.

Only 50 of the 296 patients were treated by operation, with a total mortality of 24% (12 out of 50). The mortality among those treated without operation was 43% (106 out of 246). Of these 106 deaths, 38 (36%) occurred during the first 48 hours after admission. The surgical mortality among the patients operated upon

|| References 1, 2, 16, 17, and 18.

¶ References 19 and 20.

within three days after admission was two out of nine, and the surgical treatment in these two patients had consisted only of injecting the esophageal varices with sclerosing solution. There is no advantage in delaying operation once the indications are clear and proper preoperative preparations have been made.

Death was attributed to hemorrhagic shock in 99 of the 118 patients who died (84%).

In this small group of surgically treated patients, there was no statistically significant difference between the mortality rate of the group less than 50 years of age and that more than 50 years of age. The data suggest that postponement of operation is a more important factor than age alone in affecting the surgical mortality.

The follow-up histories of 149 of the 178 patients who survived this episode of bleeding are summarized.

DISCUSSION

DR. HOWARD E. SNYDER, Winfield, Kan.: Drs. Atik and Simeone have added materially to the evidence favoring surgical management of massive gastrointestinal bleeding. They have presented data on cases admitted to City Hospital of Cleveland between the years 1941-1951 and modestly have omitted reference to their experience since. Our own experience in the past five years tends to support their conclusions, particularly that "Age and delay in operation are important factors which affect the mortality rate."

The first slide presents data on 41 patients with massive gastrointestinal hemorrhage admitted to the medical and surgical services of the Snyder-Jones Clinic in St. Mary's and William Newton Memorial Hospitals in the five-year period ending Jan. 1, 1954. They meet the criteria outlined by Atik and Simeone in their definition of massive gastrointestinal bleeding. Peptic ulcer accounted for the bleeding in all but nine of these cases. Of 26 patients with duodenal ulcers, 8 were treated medically, with 4 deaths, and 18 were treated surgically, with 1 death. Of five patients with gastric ulcer or ulcers, two were treated medically, with one death, and three treated surgically, with one death. The one patient with marginal ulcer treated surgically survived. There were no deaths in the nine miscellaneous cases in which five of the patients were treated medically and four surgically.

The second slide presents ages and mortality in the peptic ulcer group. It is seen that those treated medically who died were largely in the advanced age group. Of the five patients with peptic ulcers treated medically who lived, two had subtotal gastrectomies one month later as interval operations and one, 29 years of age, was killed in an automobile accident one year later. The other two, aged 34 and 52 years, are both women.

Twenty-one patients had subtotal and one total gastrectomy. Four of the patients with subtotal gastrectomies had gastroduodenostomy or Bilroth-I type of anastomosis. Two of the 22 patients treated surgically died. The younger, aged 62, died of massive pulmonary embolism, 15 days following gastrectomy. The older, aged 74, did not have subtotal gastrectomy until 30 days after the onset of his bleeding and he died 26 hours after surgery, presumably of ventricular fibrillation.

We believe that a single massive gastrointestinal hemorrhage from ulcer in a person past 50 years of age should constitute an indication for emergency surgery; under the age of 50, those who have continued or repeated bleeding should have emergency surgery; continued massive gastrointestinal bleeding from an undetermined cause warrants surgical exploration.

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SEVERE HEMORRHAGE IN PRESUMED PEPTIC ULCER

Surgical Treatment in the Absence of Demonstrable Lesion

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AT THE Presbyterian Hospital of Chicago, from January, 1950, to June, 1953, there were 140 cases of peptic ulcer in which gastric resection was done. Eleven patients were operated on for severe hemorrhage. In five of these no source of bleeding was found at exploration. This report is of these five cases. The nature of the lesions and the results of treatment are presented, and a program for surgical treatment of such cases is proposed.

REPORT OF CASES

CASE 1.—(W. H., Admitted Oct. 12, 1952; died Oct. 18, 1952.) A 73-year-old retired white man had had four admissions during the previous nine years, once for suprapubic prostatectomy and tonsillectomy and three times for medical observations of focal cerebrovascular accidents. On the morning of the latest hospital admission, he had suddenly passed large amounts of grossly bloody stools, followed by a massive hematemesis of bright-red blood. The patient fainted in the bathroom after this episode of hematemesis. On admission to the hospital he was not in shock. Blood pressure was 112/70; pulse rate 70 beats a minute. There was no previous history of ulcer or of episodes of melena or hematemesis. Whole blood, 500 cc., was given and ulcer management started. The hemogram showed 9.8 gm. of hemoglobin, 2,600,000 RBC, and hematocrit reading 33%. Twelve hours after admission he suddenly passed 500 cc. of grossly bloody stool, and he was given another transfusion of 1,000 cc. of whole blood.

On the second day of hospitalization the patient was found unconscious in a pool of bright-red blood (1,000 cc. estimated) which had issued from the mouth and the nostrils. The blood pressure was unobtainable, and he had a typical grand mal convulsion. During the next 12 hours 3,000 cc. of whole blood was transfused to stabilize the blood pressure and combat the exsanguinating effect of numerous passages of bloody stools and frequent hematemeses. The electrocardiogram suggested the onset of auricular fibrillation, but the rhythm became regular with rapid intravenous digitalization.

When the hemogram was stabilized momentarily at 12 gm. of hemoglobin and 4,000,000 red cells, exploration was done with the use of combined local and supplementary general anesthesia. The anesthesia was complicated by temporary respiratory arrest. The stomach was distended to the size of a football by approximately 1,000 cc. of clotted blood, which was evacuated through a gastrotomy incision. A finger was passed easily through the duodenum, revealing no bleeding point or ulcer. The stomach was visualized directly except for a small area in the fundic and cardiac portions, and no bleeding point was found. A two-thirds gastric resection was done in the hope that the bleeding point would be included in the resected organ. The patient received an additional 3,000 cc. of whole blood during surgery.

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The immediate postoperative period was complicated by paroxysmal coughing and difficult breathing; a tracheotomy was performed to facilitate respiration, and large amounts of thick mucous secretions were aspirated. The patient progressed satisfactorily until the third postoperative day, when he passed 500 cc. of grossly bloody stool. Coffee-ground material appeared through the Levin tube. For the next 24 hours the patient continued to experience frequent grossly bloody stools, and the bright-red blood in the Levin-tube drainage totaled over 2,000 cc. Whole blood, 3,000 cc., was transfused rapidly. The temperature climbed steadily to 105 F., and the patient died on the fourth postoperative day.

At autopsy the gross examination failed to reveal any lesion. However, after formalin fixation a shallow ulcer was located 7 cm. from the cardia along the greater curvature with an eroded blood vessel at the bottom of the minute crater (Fig. 1). There were associated findings of old healed cerebral and cerebellar infarcts and areas of encephalomalacia. There were healed myocardial infarcts, and the lungs showed evidence of congestion and pneumonia.

CASE 2.—(J. C., first admission March 2, 1950; discharged March 6, 1950.) A 66-year-old white male janitor was apparently well until three weeks prior to admission, at which time he experienced sharp substernal chest pains, radiating to the right upper quadrant, associated with

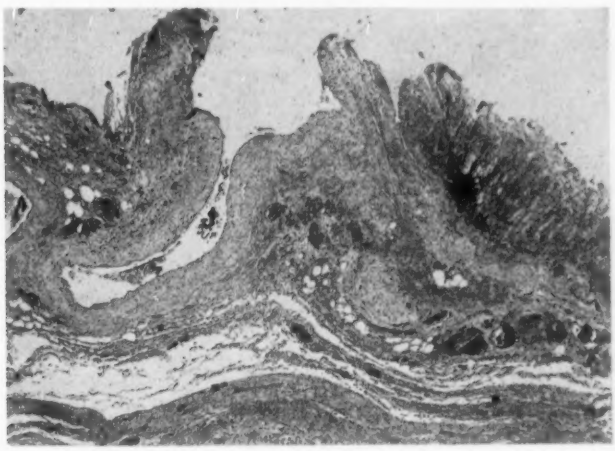

Fig. 1 (Case 1).—Photomicrograph of section through ulcer base and eroded vessel.

fainting immediately after passage of tarry stools. The substernal pains preceded the fainting spells. The history revealed an intolerance to fatty foods and a heavy daily alcoholic intake for the past 20 years. The hemoglobin content was 10 gm. per 100 cc., the RBC 2,600,000 on admission, and the electrocardiogram and gall bladder, stomach, and colon studies were reported as normal. There was a 3+ reaction for occult blood in the stools. The patient was discharged on the fifth hospital day on hematinic therapy.

(Second admission Sept. 13, 1951; discharged Oct. 24, 1951.) Two hours prior to arrival at the hospital the patient had a massive hematemesis (approximately 1,500 cc. of bright-red blood). The hemogram was 8.8 gm. of hemoglobin, RBC 2,640,000, hematocrit 29%, and prothrombin 60%; platelet counts were normal. The patient was in shock and was pale, with cold extremities. He appeared "bled out." The blood pressure was 104/68 and pulse rate 72 a minute. A diagnosis of bleeding peptic ulcer was made, and ulcer therapy was instituted. During the first week of treatment 1,500 cc. of whole blood was transfused, and the hemogram improved to 10 gm. of hemoglobin and RBC 3,300,000. However, the patient continued to have a 3+ reaction for occult blood in the stools. Seven days after admission a large quantity of tarry stool was passed and the patient fainted in the bathroom. The blood pressure fell to 78/42; the hemoglobin to 7 gm., and the red cell count to 2,600,000. The hematocrit was 25%. Whole blood,

1,000 cc., was transfused immediately, and the blood pressure was stabilized momentarily at 90/60. The patient continued to pass large amounts of bloody and tarry stools, and within 48 hours he was in shock. Administration of 4,000 cc. of whole blood in 48 hours failed to improve the shock, and operation was decided on, since it was obvious that massive exsanguinating hemorrhage was continuing. The patient came to the operating room cold and clammy, with a blood pressure of 80/60.

At operation the stomach was distended with blood clots, which were evacuated through a gastrotomy incision. However, no active bleeding source could be visualized, and palpation of the duodenum revealed no induration. The stomach was inspected minutely along the accessible lesser and greater curvatures, and a finger was passed up the cardiac sphincter. Because visualization of the fundus and esophagogastric junction was incomplete, esophagoscopy was performed on the operating table, and at 33 cm. from the incisor teeth a small esophageal diverticulum was reported by the esophagoscopist. The esophagus was free of lesions otherwise. In view of these findings, the gastrotomy was closed without resection.

On the fourth postoperative day sudden sharp epigastric pain, with aspiration of 70 cc. of bright-red blood through the Levin tube, occurred. In the next eight hours the patient went into

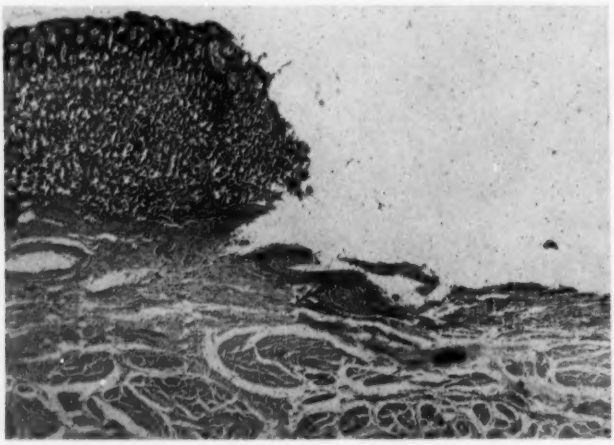

Fig. 2 (Case 2).—Photomicrograph of section of superficial ulcer, showing edge of ulcer and abrupt transition from mucosa to ulcer with absence of any chronic inflammatory changes.

shock, and 1,000 cc. of mixed blood clots and bright-red blood were aspirated by means of a Levin tube. In spite of the administration of 2,000 cc. of whole blood, the hemogram remained at 9.5 gm. of hemoglobin and 3,670,000 red cells, associated with a blood pressure of 70/50. Under the impression that varices might have been missed on the first examination, esophagoscopy was performed again and was negative. Sulfobromophthalein test showed 6.8% retention at 45 minutes; the Hanger test was negative, and the prothrombin 72%. From the 13th to the 19th postoperative day the patient continued to experience hematemesis of coffee-ground to bright-red blood in amounts varying from 30 to 60 cc. A stomach fluoroscopy at this time showed a duodenal deformity. The bleeding and clotting times were normal. On the 19th postoperative day there was hematemesis of approximately 1,000 cc. of bright blood, and shock supervened. Two liters of blood was transfused within the next 24 hours. The patient was taken to the operating room. A two-thirds resection was performed. The pathologic report described a gastric ulceration 3.5 cm. by 3 mm. in the site of the previous gastrotomy incision in the resected specimen. The patient was discharged on the 12th postoperative day after an uneventful course.

(Third admission Oct. 25, 1951; died Nov. 3, 1951.) Twenty-four hours after the patient's discharge on the 12th postoperative day, he was readmitted in shock. The blood pressure was

68/60, the pulse rate 90 a mniute, and respirations 8 a minute. Whole blood, 1,000 cc., was rapidly transfused, and the blood pressure rose to 112/60. During the next seven days the patient continued to pass grossly bloody stools and he vomited bright-red blood, and in spite of an additional 1,000 cc. of whole blood he gradually went downhill and died in shock on the eighth hospital day.

At autopsy a superficial ulceration 3.5 cm. from the cardia near the lesser curvature was found with a centrally located open vessel, plugged with a recent thrombus (Fig. 2). Dark blood could be expressed from the open vessel. The esophagus and remaining 8 cm. long gastric pouch disclosed no other source of bleeding which might account for the exsanguination.

CASE 3.—(R. S., first admission March 6, 1952; discharged March 20, 1952.) A 47-year-old patient was first seen with a previously diagnosed duodenal ulcer (demonstrated by x-rays) one month prior to admission. During the year preceding admission, he had suffered frequent spells of vomiting, epigastric distress, and fatigability. Melena had occurred several times, and the hemogram was 2,600,000 RBC, 8.3 gm. of hemoglobin. The patient had a past history of excessive drinking. He was discharged after two weeks with a diagnosis of heart disease of unknown etiology, cardiac decompensation, hepatomegaly, and duodenal ulcer with severe secondary anemia.

(Second admission Nov. 16, 1952; died Dec. 5, 1952.) Eight months later he was readmitted for persistent anemia and gradually falling blood count from a bleeding duodenal ulcer. The patient had been given ulcer and cardiac management and had been receiving liver and iron. Physical findings included ascending thrill along the carotids, systolic aortic murmur, and Grade 3 systolic murmur along the left sternal border. A_2 was absent, and P_2 was accentuated. The liver edge was 1 fingerbreadth below the costal margin. A diagnosis of aortic calcific stenosis with regurgitation and active bleeding duodenal ulcer was made.

Two thousand cubic centimeters of blood was transfused in preparation for an elective subtotal gastric resection. On the fifth hospital day surgery was carried out and a two-thirds gastric resection was performed. At surgery no duodenal induration was noted. The liver was normal in appearance. The postoperative progress was uneventful until the sixth postoperative day, when the patient experienced a sudden profuse hematemesis (650 cc. of bright-red blood). The abdomen remained soft, and the blood pressure was maintained at 150/90 with a transfusion. On the seventh postoperative day a massive hematemesis of approximately 700 cc. of bright blood and clots occurred, followed closely by another hematemesis of 400 cc. The patient was treated immediately by 1,000 cc. of transfused whole blood. During the next 24 hours he continued to vomit blood and clots in varying amounts of 50 cc. to 700 cc. Shock was treated by transfusion of 3,000 cc. of whole blood, and, after 18 hours of intermittent hematemesis, totaling approximately 2,000 cc., an exploratory laparotomy was undertaken with the use of local and supplementary inhalation anesthesia.

At surgery there was an occult dehiscence of the wound with protrusion of intestinal loops through the posterior sheath and marked distention of the remaining gastric pouch with a large blood cast which was removed through a 5 cm. gastrotomy incision. No bleeding point could be identified after careful and thorough inspection and palpation through the gastrotomy incision. The gastrotomy incision was closed and the exploration terminated. During the first two postoperative days an additional 2,000 cc. of blood was transfused, and bleeding seemed to have ceased. The hemogram was 3,700,000 RBC, 12.5 gm. of hemoglobin, and hematocrit value 40%. Suddenly, on the second postoperative day, large amounts of bright-red blood and tarry clots were passed per rectum, followed 18 hours later by another copious bloody movement. The Rumpel-Leede phenomenon, and bleeding and clotting times were normal. The patient died in coma.

At autopsy there was a superficial ulceration 4 cm. from the esophagogastric junction and an area of erosion just above the gastrojejunal anastomotic line. An interesting finding was vegetations of the aortic valve.

CASE 4.—(W. W., first admission Jan. 12, 1953; discharged Jan. 31, 1953.) Twenty-four hours prior to admission, a 63-year-old white chemist, in apparent good health, passed two

copious bloody stools, associated with faintness and dizziness. There was no preceding history of peptic ulcer or varices. The patient's father and brother both suffered from peptic ulcers. The patient admitted taking sodium bicarbonate for dyspepsia. The physical examination was negative except for tenderness to deep pressure in the right abdomen. A diagnosis of bleeding peptic ulcer was made, and the patient was given ulcer therapy.

During the next 72 hours the patient again passed copious amounts of grossly bloody stool which soaked the bed linen and towels. The hemogram fell to 7.5 gm. of hemoglobin, 1,790,000 RBC, and 23% reading on the hematocrit. Whole blood, 3,500 cc., was transfused during this period, but the blood picture failed to respond. The patient was taken to surgery for exploration to find the bleeding point.

At operation the entire gastrointestinal tract was distended with clotted blood, extending from the stomach to the transverse colon, in which pieces of clots were visible. No palpable lesion was found in the stomach. A duodenotomy revealed a questionable area of duodenal erosion, located over the pulsating pancreaticoduodenal artery. In the hope of including the bleeding

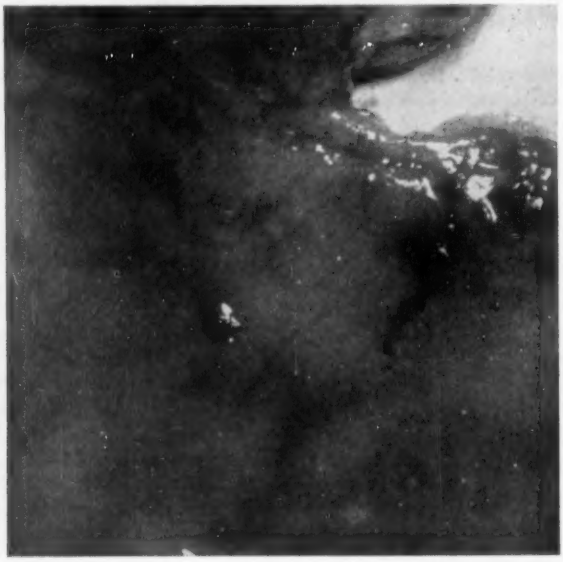

Fig. 3 (Case 5).—Photograph of gross specimen, showing gastric erosions.

point, a two-thirds subtotal gastric resection was performed. All signs of bleeding disappeared after surgery, and after multiple transfusions the blood picture improved to the point that on his discharge, on the 16th postoperative day, the hemoglobin was 11.5 gm. and the RBC, 3,750,000.

The pathological report of the resected stomach described "mild gastritis—intact gastric and duodenal mucosa—histological evidence of extensive recent hemorrhage into the gastric muscularis."

Six weeks after discharge this patient was readmitted for passage of large tarry stools six hours previously. On admission the patient was comfortable but pale, and the hemogram was 9.5 gm. of hemoglobin, 2,900,000 RBC, and 38% the hematocrit reading. The possibility of a bleeding marginal ulcer was considered, and the patient was given ulcer therapy. Twenty-four hours after admission the patient again passed a large tarry stool, and the blood values fell to hematocrit reading of 29%, 7.5 gm. of hemoglobin, and 2,800,000 RBC. Multiple transfusions continued. The prothrombin and bleeding and clotting times were all normal. Roentgen studies revealed no evidence of marginal ulcers, esophageal varices, or polyps of the bowel. The esophagoscopy was negative. Bleeding stopped gradually, and the patient was discharged on the 13th

hospital day, with absence of occult blood in the stools. He has had recurrent bleeding two and nine months after discharge.

CASE 5.—(G. M., admitted March 26, 1953; discharged April 17, 1953.) Three hours prior to admission, a 64-year-old white bank employee had a sudden hematemesis on the street and a second hematemesis while being admitted in the emergency room. There was a history of epigastric fullness and distention four days prior to admission, and 18 years previously the patient

TABLE 1.—*Summary of Data*

	AGE	LOWEST RECORDED BLOOD VALUES	INTERVAL BEFORE SURGERY	SURGICAL PROCEDURE	RESULTS
CASE 1	73	RBC: 2.6 mill. Hb: 7.5 gms. % Crit.: 33 %	48 hrs.	2/3 Resection	Died. Shallow ulcer with open blood vessel 7 cm. from Cardia.
CASE 2	66	RBC: 2.3 mill. Hb: 7 gms. % Crit.: 29 %	9 days	2/3 Resection, Esophagoscopy	Died. Shallow ulcer 3.5 cm. from Cardia
CASE 3	47	RBC: 2.8 mill. Hb: 7.5 gms. % Crit.: 29 %	1st Admiss. 5 days 2nd Admiss. 8 days	2/3 Resection, Explor. laparotomy	Died. Shallow ulcer 4 cm. from Cardia.
CASE 4	63	RBC: 1.79 mill. Hb: 7.5 gms. % Crit.: 23 %	72 hrs.	2/3 Resection	Melena 6 wks. later; gradual cessation of bleeding.
CASE 5	64	RBC: 2.7 mill. Hb: 8.5 gms. % Crit.: 26 %	48 hrs.	3/4 Resection, Vagotomy	Well. Multiple erosions and gastritis.

TABLE 2.—*Summary of Data*

	PREVIOUS ULCER HISTORY	HEMATEMESIS	MELENA	SHOCK	UNITS (500 cc.) BLOOD TRANSFUSED
CASE 1	No	Massive	Gross	Yes	34
CASE 2	No	Massive	Gross	Yes	1st Admiss. 30 2nd Admiss. 8
CASE 3	Yes	Massive	Gross	Yes	16
CASE 4	No	0	Gross	Yes	9
CASE 5	Yes	Massive	Gross	Yes	6

had experienced gross gastric hemorrhage for which he had been hospitalized and received ulcer treatment, which included mucin from hog's stomach. There had been various courses of antacids, including Tums and sodium bicarbonate from time to time. The alcohol intake was heavy.

When received in the emergency room the patient was cold and clammy but not in shock. The blood pressure was 162/80, pulse rate 88 beats a minute, and hemogram was 11 gm. of hemoglobin, 3,350,000 RBC, and 29% hematocrit value. Transfusions of whole blood were started. Three hours later a large hematemesis filled one basin with bright-red blood clots. There was concomitant passage of bloody stools. Four hours later his blood pressure had fallen to 116/60, and the patient was cold and faint. One thousand cc. of whole blood was given in 45 minutes. During the first 12 hours of admission the patient received 3,000 cc. of whole blood. He was taken to the operating room, where exploration revealed only mild induration in the site of the old duodenal ulcer. Duodenotomy revealed no bleeding point. One thousand cubic centi-

meters of blood was administered during operation, and a three-fourths subtotal gastric resection and subdiaphragmatic vagotomy was performed after gastrotomy revealed multiple gastric erosions. The patient recovered uneventfully, with cessation of bleeding, and he was discharged on the 19th postoperative day. He has remained well.

Examination of the resected specimen showed atrophic gastritis and multiple superficial erosions (Fig. 3).

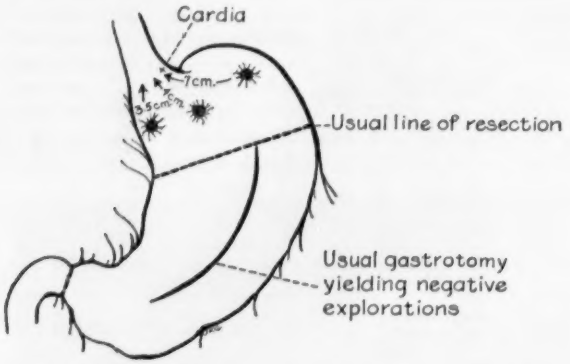

Fig. 4.—Location of exsanguinating hemorrhages: sites of the bleeding points which could not be located in the first three cases.

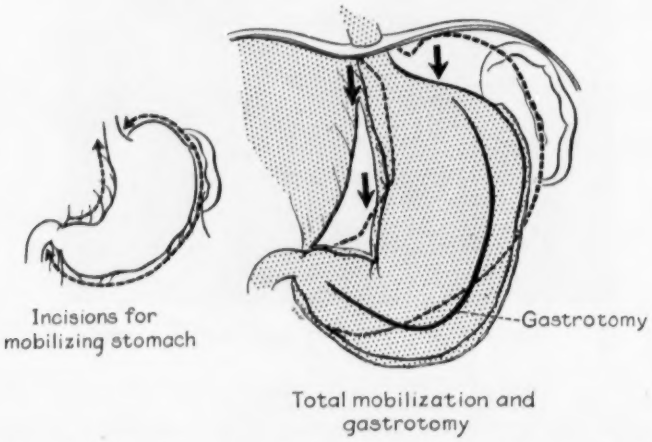

Fig. 5.—Showing how the stomach can be mobilized downward by division of all the vessels entering the stomach. This allows for more thorough inspection of the upper pouch of the stomach through the gastrotomy incision and also allows for more extensive resection.

COMMENT

Since 1898, when Dieulafoy described fatal hematemesis from superficial "exulcerations" within 2 cm. of the esophagus, the possibility of high cardiac lesions must be entertained in unexplainable massive gastric hemorrhage. The three fatal cases reported here had bleeding areas in the gastric mucosa 3.5 to 7 cm. from the esophagus (Fig. 4). The experiences of the three surgeons, just described, emphasized the necessity to rule out these lesions. The anatomical basis for the profuse bleeding

in superficial ulcers and erosions is found in the extensions of these lesions into the intensely vascular submucosal and mucosal plexuses.

The definitions of massive bleeding and the necessity for surgical intervention are, among others, shock, syncope, and rate of blood loss requiring more than 1.5

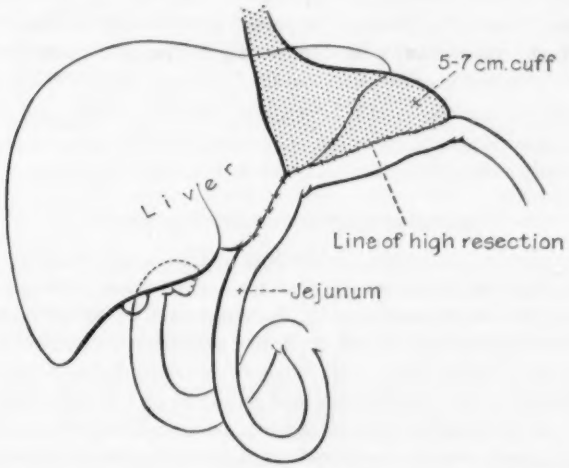

Fig. 6.—Showing the amount of stomach remaining at the end of the usual operation when the bleeding point is not found.

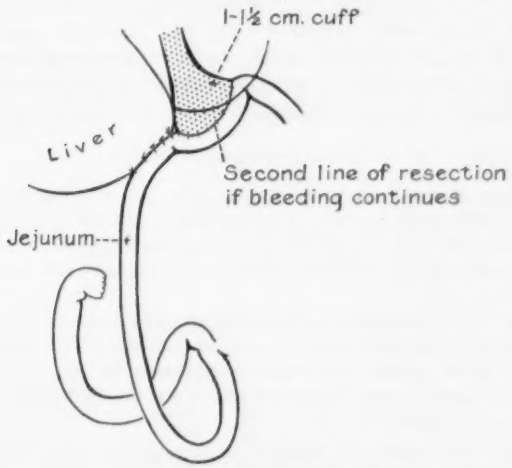

Fig. 7.—Suggested amount of stomach which should be left when operating on a patient who continues to bleed after the usual 75% resection.

liters replacement in 24 hours, as defined by Hoerr, Dunphy, and Gray; a fall in red cell count to 2,500,000 or less, and a reduction to 60% or less in circulating red cell volume, as defined by Stewart and his associates. We believe that patients who fall in these categories should have rapid transfusions with whole blood to abolish

shock and to return the blood values to normal before surgical intervention. However, if bleeding recurs or there is failure to stabilize with transfusions, immediate exploration is indicated. Especially is early exploration imperative in patients more than 45 years of age. Many authors have described the increased mortality rates in these patients who are past 45 years of age.

Exploration in massive bleeding of peptic ulcer usually discloses the bleeding site. However, our experiences with this group of five cases of undetermined bleeding site, in which three of the cases ended fatally, is unique in our hospital.

Stewart and his associates, and Wangensteen, Bentley, Cooper, and Ferguson have reported high resections with cessation of bleeding in most patients operated on for severe hemorrhage when the lesion was undiscoverable at operation.

RECOMMENDED SURGICAL TREATMENT

On exploration for a source of bleeding which is not evident, the clots are removed from the distended stomach through a gastrotomy incision, extending to within 7 cm. of the esophagus (Fig. 5). Careful search of the accessible mucosa is made. If no bleeding source is found, the entire stomach is mobilized by freeing both curvatures and ligating all vessels, permitting a downward displacement of the fundus (Fig. 5). This will allow visualization and palpation of the entire mucosal surface. With failure to demonstrate a definite bleeding source, a 75 to 80% resection is done. If peptic erosions are present, an infradiaphragmatic vagotomy is performed at the same time (Fig. 6).

After resection, should massive hemorrhage recur, reoperation is recommended, at which time the remaining stomach is resected except for a narrow 1.5 cm. cuff, the mucosa of which can be easily visualized (Fig. 7). We know of one such instance in which reoperation and resection of all the stomach except for a 1.5 cm. cuff resulted in cessation of bleeding in spite of the lack of any demonstrable bleeding lesion in the segment of stomach resected at the second operation.

DISCUSSION

DR. H. S. MORTON, Montreal, Canada: I should like to discuss the second paper on bleeding from the stomach of undetermined origin. It is very seldom that one has an opportunity to discuss this subject, and first of all, I should like to consider the etiology. For convenience, may I suggest the term "gastrostaxis," or a diapodesis of the red cells through the mucosa, instead of the long phrase already used.

In the February, 1954, issue of *Surgery, Gynecology and Obstetrics*, in the abstract section, page 144, Wachsmuch is quoted as having reported four cases of bleeding and performed experimental work on 45 rabbits. The vagus is stimulated by means of methamphetamine (Pervitin), histamine, and acetylcholine, which produced hemorrhage from the stomach, intestine, and occasionally from the kidney.

In discussing this problem with Dr. Webster, in Montreal, he stated that in the laboratory, overstimulation of the vagus will produce bleeding from the stomach or the bowel. Therefore the etiology would seem to be associated with stimulation of the vagus. In a recent review of 15 cases at the Royal Victoria Hospital during the last 10 years, there were only two deaths from this cause, and the usual treatment was subtotal gastric resection.

Regarding the diagnosis of this condition [Slide] by means of the electrogastrograph, we have had an opportunity to diagnose three such cases. In order to orientate you, the first slide is one of a normal electrogastrogram combined with a tambour recording. The amplitude of the three cycles per minute is 1 mv.

[Slide] This slide shows acute gastric erosions with hemorrhage, and the three waves per minute are regular, and have an amplitude of 10 mv. Therefore, from both experimental and clinical knowledge, it would seem that we should think of using vagotomy in addition to subtotal gastric resection. The patient on whom this last recording was taken had had massive bleeding. On exploration, no abnormality was found. He continued to bleed afterward, when this recording was made. He then had a subtotal resection and, in my opinion, should have had a vagotomy as well. We have three such cases.

Dr. E. T. Thieme, Ann Arbor, Mich.: I should like to discuss briefly the problem so well presented by Dr. Chun, namely, the problem faced by the surgeon, who, in operating for uncontrolled hemorrhage, can find no lesion in the stomach or duodenum.

Recently, we published a brief report emphasizing the importance of gastric erosions in this problem. Gastric erosions were probably first described by Gallard, who presented two cases that exsanguinated despite the use of ergot, white wine, and rum. After the specimens were fixed, there was a typical gastric erosion, as so well presented by Dr. Chun, seen quite clearly. Since that time relatively little has been published concerning this except in the reports mentioned by Dr. Chun.

In our experience, in 11 patients operated upon for uncontrolled hemorrhage recently, 4 had a duodenal ulcer, 3 had a gastric ulcer, and in 4 no lesion was found. Gastric resection was undertaken immediately without gastrotomy, and the patients made an uneventful recovery as far as any further bleeding was concerned. There was one fatality on the 14th hospital day, cause unknown.

Therefore, we feel that when you encounter this problem gastrotomy probably will be of very little help, and gastric resection should be done immediately. These lesions are too small to be seen by the naked eye. They cannot be felt, and they cannot be demonstrated by x-rays. Therefore, we have made it a policy to do immediate gastric resection without gastrotomy.

In our experience, these lesions have followed the expected pattern of location of gastric ulcers. Therefore, a high gastric resection included all four lesions. I am unable to explain the marked difference between our experience and that of Drs. Chun and Gilchrist.

Dr. Jacob K. Berman, Indianapolis: Drs. Chun and Gilchrist have given us a very important and timely report.

We have had three patients with the erosive gastritis syndrome, or what was formerly known as the erosions of Dieulafoy. All of these patients have been more than 60 years of age; two were women, aged 72 and 62, and one, a man, was a physician aged 67; all had almost total gastrectomy and all recovered.

I should like to make just a few comments concerning one of our patients, because Dr. Gilchrist saw this woman, and I imagine that she is the one to whom Dr. Chun referred.

Miss I. J., aged 62 years, came to the hospital in an exsanguinated state. She had been vomiting and passing large quantities of blood by rectum for about four days and the hemoglobin content was 5 gm. per 100 cc. Our diagnosis was bleeding duodenal ulcer. We restored the blood volume, but hematemesis and melena continued, and, therefore, we decided that immediate surgery was indicated.

At operation there appeared to be a superficial ulcer on the proximal side of the pylorus, and a conventional subtotal gastric resection was done. The pathologist thought that the mucosal ulcer was an artefact. The patient's immediate postoperative course was excellent. However, on the sixth day she began vomiting blood, and the stools were almost pure blood. Blood replacement continued, but the hemorrhage was so profuse that it was difficult to keep the blood volume within normal limits. A total of 13,500 cc. of whole blood, and 43,500 cc. in the form of plasma expanders, electrolyte, and dextrose solutions were given.

We thought that perhaps the bleeding point was in the suture line, and therefore reexploration was done. However, we found that the suture line was intact. Moreover, no definite site of hemorrhage could be identified. We performed a very extensive gastrectomy, as suggested by Dr. Gilchrist, and the patient recovered and has remained well. However, our pathologist has not as yet determined the cause of the massive hemorrhage.

As a result of this experience, as well as the two previous cases mentioned, I believe that patients with gastric hemorrhage without demonstrable cause should have almost total gastric resection.

DR. CHARLES G. JOHNSTON, Detroit: Any major episode of bleeding from the upper gastrointestinal tract is a surgical problem and should be seen and handled by the surgeon. The treatment of ulcer in most instances is another matter, but we should not confuse the treatment of the ulcer and the treatment of hemorrhage, as they are different problems and not necessarily related. If we want to differentiate between surgical and nonsurgical treatment of bleeding, that is another matter. Even here this is shady wording because the means and methods of stopping hemorrhage in the upper gastrointestinal tract presents problems similar to bleeding elsewhere. The fact that the bleeding vessel is not easily seen may cause us some difficulty; the basic problem is just the same.

DR. WILLIAM D. HOLDEN, Cleveland: I should like to make one or two comments about this extremely difficult lesion. It is what many have called acute mucosal ulceration of the cardia of the stomach, and I think every surgeon who treats gastric hemorrhage sooner or later encounters one of these patients.

As to the etiology of this type of ulceration, I am not sure that we should call this a peptic ulcer. I do not know the etiology. However, we have looked into the histories of the few patients that we have seen who have had this type of ulceration, and not infrequently there is a history of trauma associated with the onset of the massive hemorrhage—trauma in the form of violent coughing or retching.

Some of these patients have started to bleed without any history of previous upper gastrointestinal disease and during the course of a severe upper respiratory infection. I do not know that the trauma itself really contributes etiologically to the development of these mucosal ulcerations, but I think it is possible.

One other point is important because I have seen this occur on two occasions. The abdomen has been explored for presumed peptic ulceration during the course of massive bleeding, and a chronic duodenal or pyloric ulcer has been encountered. A gastric resection has been carried out in the usual way.

The patient has had (in addition to the chronic pyloral-duodenal ulcer that was not bleeding) an acute mucosal ulcer along the lesser curvature of the cardia and has gone right on and bled to death from the ulcer that was completely unsuspected at the time of operation.

One of the discussants mentioned that roentgenographically one cannot demonstrate these ulcers. That has been our experience. Neither can we demonstrate these ulcers by palpation at the operating table. Unless you can see it, you will very often never suspect it exists. On one or two occasions we have been able to introduce a proctoscope through a small opening in the stomach and see a small bleeding mucosal ulcer in the cardia of the stomach. I do not believe that that maneuver is going to demonstrate all of these ulcers, but occasionally it may be of some benefit.

DR. R. K. GILCHRIST, Chicago: This discussion has demonstrated the reason for our having prepared this paper. I want to reiterate just a few principles.

First, I might say that of some 200 cases that were reviewed recently at Cook County Hospital, in approximately half of those operated on for acute massive hemorrhage, no bleeding point was found.

The first case I probably should not have operated upon. Dr. Holden mentioned the cough. I am sure that started the hemorrhage on the third day, because the man had had a chronic cough for years, and he really did cough hard.

When you operate on such a patient, if there is blood in the stomach and no sign of any other cause of hemorrhage, resection should be done. In my opinion the entire stomach should be mobilized and all the blood supply to it cut, so that you can bring the entire upper pouch of the stomach down, which makes a very easy resection. If there are gastric erosions, the patient should have a vagotomy at the same time.

If the patient bleeds after surgery, in my opinion, and if the bleeding is very hard, reexploration should be done; as Dr. Berman said, the resection should be done early, because I feel quite sure that we are having patients die after surgery who could be saved if the surgeon had already made up his mind that he was going to reoperate.

In the first case I had, I know I would have reoperated upon the patient except that he was in such a poor condition that I did not have nerve enough to do it.

DR. NEWTON CHUN, Chicago: I want to thank the discussants. It behooves the operator to rule out these high-lying peptic lesions in massive bleeding from undiscoverable gastroduodenal origin. Students of this subject have emphasized the essentially benign nature of most of these lesions, in which as many as 25 hemorrhages have occurred with survival. However, with a patient more than 45 years of age, in shock, and bleeding massively from an organic erosion of a blood vessel, such lesions can be amenable only to radical surgery.

Lesions mentioned in this discussion which were associated with vomiting have been previously described by Weiss, the so-called Mallory-Weiss syndrome, in which violent vomiting initiated longitudinal tears at the esophagogastric junction. Such lesions must be distinguished from these high-lying cardiac ulcers.

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MASSIVE POSTOPERATIVE HEMORRHAGE DUE TO UNRECOGNIZED THROMBOCYTOPENIA

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OMAHA

THE CLINICAL significance of acute and chronic thrombocytopenic purpura has been well understood for many years. The simultaneous occurrence of such a condition during the immediate postoperative period presents additional problems which require prompt recognition and careful treatment. Our recent experience with seven such cases has focused our attention on this particular problem.

The function of the platelets in circulating blood was recognized and described by Bizzozero in 1882. He demonstrated their adhesive qualities, participation in thrombi, and the role in the coagulation of blood. The actual origin of these platelets has been the subject of much speculation, but Wright in 1906 suggested that they were formed in the bone marrow from megakaryocytes. He concluded that the platelets represented detached bits of cytoplasm of the megakaryocytes.[9] There are roughly 100,000 of these platelets formed and destroyed each day, and the entire number in the circulating plasma can be replaced in from three to five days.

Normally 250,000 per cubic millimeter are found in the circulating plasma, and in addition they are seen in the spleen, in the liver, and particularly in the lungs. In the circulating blood they function by direct sealing of the open vessel by agglutination and simultaneously liberate thromboplastin, which initiates coagulation.[9]

The number of platelets in circulating plasma changes with physiological variations. There is a daily fluctuation of from 6 to 7%. Newborn babies have lower platelet counts during the first 48 hours. Menstruation decreases the platelets from 50 to 75% on the first day, these increasing to normal by the fourth or fifth day. There is no change seen in pregnancy. Violent exercise or a change in posture will cause appreciable change in platelets. In many disease states there are also changes, and a thrombocytopenia may exist. Trauma and asphyxiation cause a sharp increase. Platelet counts increase from 30 to 100% after surgical operations, and the maximum rise is noted from the 7th to the 20th day.[9]

The exact mechanism of postoperative thrombocytosis is difficult to understand, because it is so long delayed. One hypothesis suggested is that it is the result of absorption of necrotic material and exudate from the wound. The degree of rise can only roughly be correlated with the extent of the surgery done.[1]

The problem of a prolonged thrombocytopenia during the postoperative period is unusual in that normally a thrombocytosis occurs. We have had the opportunity

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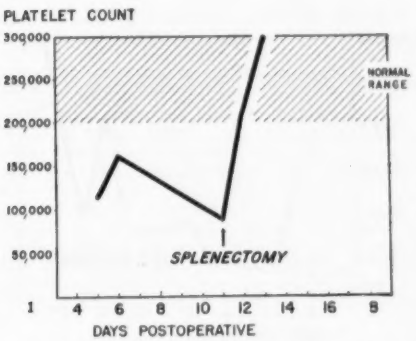
to observe seven cases in which postoperative bleeding into the operative site occurred. In each case bleeding from insecure ligation of vessels was ruled out and a definite thrombocytopenia found. The treatment of these cases varied. In four cases splenectomy was performed, with satisfactory results. In two cases supportive therapy with repeated blood transfusions was employed. In one case cortisone was given.

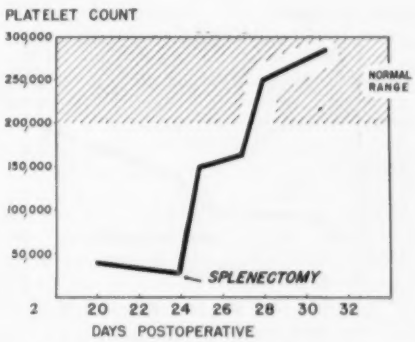
REPORT OF CASES

CASE 1.—A 24-year-old white woman developed menorrhagia which persisted for a period of three months. A diagnostic dilation and curettage were done with no ill effects. On the seventh postoperative day she developed profuse vaginal bleeding which could not be controlled. Two days later a total hysterectomy and left salpingo-oophorectomy were done. The vaginal and abdominal wound bleeding continued, although 2,000 cc. of blood was given. On the fifth postoperative day after hysterectomy the platelets were found to be depressed, and with no improvement a splenectomy was done on the 11th postoperative day.

CASE 2.—A 60-year-old white man was admitted to the hospital for treatment of a bleeding duodenal ulcer. There was a history of frequent but easily controlled epistaxis over a period



Graph 1 (Case 1).—Platelet count after it was recognized that thrombocytopenia existed. History revealed no evidence of previous bleeding tendency or toxic medications. We saw patient first on fifth postoperative day after total hysterectomy, when platelet count was 115,000. Subsequent platelet counts of 168,000 and, finally, 81,000, on 11th postoperative day, were obtained. Repeated transfusions of 500 cc. of fresh blood did not improve either platelet count or bleeding tendency, and splenectomy was done on 11th postoperative day. Platelets promptly rose to 210,000 and then into normal range, with no further bleeding. Patient was dismissed one week after splenectomy. Follow-up two years later showed no evidence of further bleeding tendency.



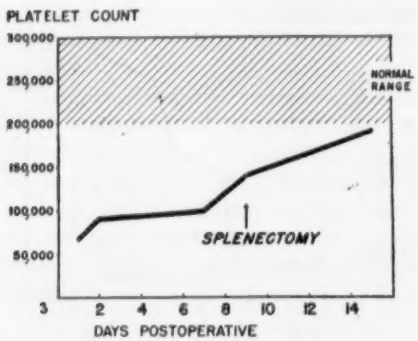
Graph 2 (Case 2).—Platelet count on patient seen first on 20th day after transurethral resection. Bleeding had continued in spite of two cystoscopies with fulguration and finally suprapubic cystostomy with fulguration. Although tourniquet test was positive, no cutaneous purpura was evident. There was no history of administration of drugs or bleeding tendency other than epistaxis. Bone marrow studies showed megakaryocytes and were compatible with thrombocytopenic purpura. Patient received repeated transfusions (4,000 cc.) of fresh blood, but platelet count remained low. On 24th postoperatvie day, platelet count was 25,000 and splenectomy was done. There were immediate cessation of bleeding and prompt rise in platelet count. Follow-up five years later showed no evidence of further bleeding tendency.

of 10 years. The bleeding duodenal ulcer was responding to conservative treatment satisfactorily when acute prostatic obstruction occurred. The urologist advised transurethral prostatic resection, which was done. Bleeding was excessive after this, and on the day of operation the bladder neck was fulgurated by cystoscopy. Bleeding continued, and the fulguration was repeated on the first day postoperatively. Bleeding slowed somewhat but continued, and the bladder was filled with clots. On the fifth postoperative day a suprapubic cystotomy was done and the

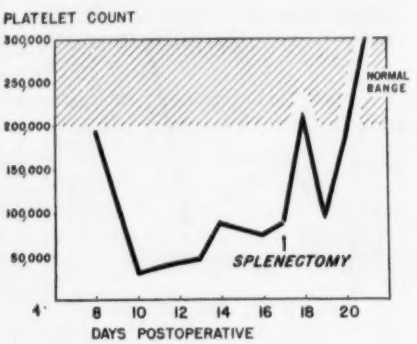
bladder neck fulgurated under direct vision. A platelet count was done at the time and found to be 80,000, and this remained consistently depressed. A splenectomy was done on the 24th postoperative day, the bleeding stopped immediately, and the patient improved.

Case 3.—A 24-year-old white woman was admitted with a history of menorrhagia. There was a history of some previous bruising, but an appendectomy four years before and a delivery six years before were accomplished without difficulty. Dilatation and curettage were done, followed by a pelvic laparotomy with ligation and severing of both ovarian pedicles, presacral neurectomy, and uterine suspension. At operation abnormal oozing was noted; this prompted a platelet count, which was 70,000. On the third postoperative day moderate vaginal bleeding developed, and on the fifth postoperative day oozing was noted from the abdominal wound. This bleeding could not be controlled by conservative measures, the platelets were depressed, and a splenectomy was done on the ninth postoperative day, with satisfactory recovery.

Case 4.—A 42-year-old white woman was admitted with a history of irregular menses and menorrhagia of two years' duration. There was no previous history of bleeding tendency or ingestion of toxic drugs. Thyroidectomy and appendenctomy had been performed eight years previously with no difficulty. There had been four term pregnancies without any bleeding difficulty. A total hysterectomy and bilateral salpingo-oophorectomy were done. On the seventh postoperative day she developed a cutaneous purpura, vaginal bleeding, and gross hematuria.



Graph 3 (Case 3).—Although history of bruising was noted, it did not seem significant preoperatively. Bone marrow studies showed megakaryocytic activity compatible with essential thrombocytopenic purpura. There was no history of ingestion of toxic drugs. Follow-up two years later showed no recurrence of bleeding tendency.



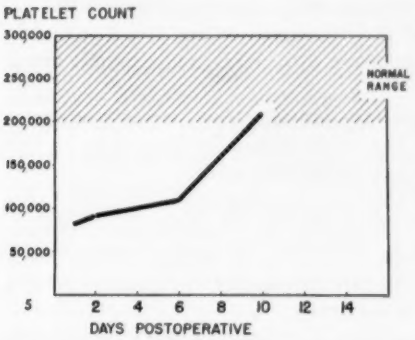
Graph 4 (Case 4).—Postoperative course was uneventful until seventh postoperative day, at which time bleeding developed. Platelet count was almost within normal range at this time, 193,000, but fell on subsequent days. Patient failed to improve and continued to bleed until splenectomy was done on 17th postoperative day. Platelet count at that time was 80,000. After splenectomy platelets rose to 216,000, dropped back to 90,000, and then continued up into normal range. There was no clinical evidence of bleeding after splenectomy.

An intravenous pyelogram revealed no abnormalities of the kidneys. On the 17th postoperative day a splenectomy was done, and the bleeding subsided.

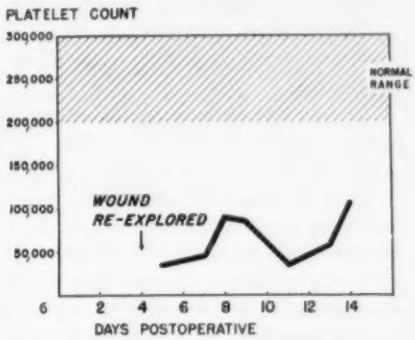
Case 5.—A 39-year-old white woman was admitted with irregular menses and menorrhagia. There was a history of bruising, but a thyroidectomy had been done 10 months previously without difficulty, although an ecchymosis developed over the lower neck. She had an alcoholic cirrhosis and an enlarged liver palpable 4 cm. below the costal margin. She had been on iron medication for the past six months for anemia. A total hysterectomy was done, and 1,000 cc. of blood was given during and immediately after surgery. Six hours postoperatively there was oozing from the abdominal wound.

Case 6.—A 58-year-old white woman was admitted complaining of retraction of the nipple, dimpling of the skin, and a previous history of bleeding from the nipple. There was no history

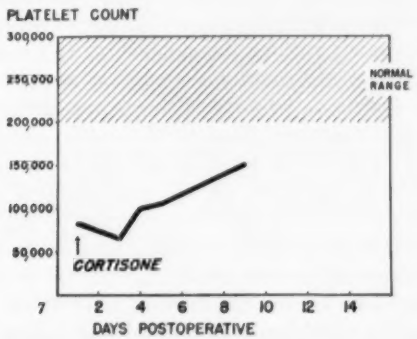
of a bleeding tendency and no history of intake of toxic drugs. A radical mastectomy was done without incident. On the third postoperative day there was considerable bleeding from the wound, with the development of a large wound hematoma. On the fourth postoperative day the wound was reexplored when it was believed that a ligature on a major vessel had loosened. Careful exploration failed to substantiate this belief, and a platelet count was done, showing 30,000 platelets.



Graph 5 (Case 5).—Abnormal oozing at time of operation prompted early check of platelets, which were found to number 77,000. After abdominal wound oozing was noted, additional 1,000 cc. of blood was given. Curve shows how platelet count gradually increased until 10th postoperative day, when it was within normal range. A splenectomy was not considered necessary, because of patient's steady improvement under conservative therapy. After last 1,000 cc. of blood she developed marked urticaria, which was relieved by antihistamines.



Graph 6 (Case 6).—When reexploration of wound was negative, platelets were found to number only 30,000. Patient received daily transfusions of 500 cc. of blood until a total of 2,500 cc. had been given. Under conservative treatment there was no evidence of further bleeding. Platelet count remained low throughout hospital course in spite of repeated fresh blood transfusions. Follow-up two years later showed no evidence of bleeding tendency.



Graph 7 (Case 7).—Patient was seen on first day after vasectomy, with platelet count of 70,000. He was started on cortisone, 25 mg. q.i.d.; no further bleeding occurred and he promptly improved.

Case 7.—A 30-year-old white man had a vasectomy done in a physician's office 24 hours previous to his admission. On admission it was found that he had developed a large scrotal hematoma, which extended up over the groin into the thigh. Hemostasis had been adequate at the time of surgery, and careful exploration failed to reveal any bleeding vessel. Although there had been some bleeding from a tooth extraction several years earlier, there was no

other history of a bleeding tendency. There was no history of drug administration. Tourniquet test was negative. Sternal marrow was essentially normal, with hyperplasia of megakaryocytes compatible with thrombocytopenic purpura.

Four of these operative procedures were on the pelvis. One was a pelvic laparotomy with uterine suspension, ligation of ovarian pedicles, and presacral neurectomy. Two were total hysterectomies for menorrhagia. One was a total hysterectomy done shortly after a diagnostic dilatation and curettage with excessive hemorrhage.

Two of these operative procedures were of a urological nature, one a prostatectomy, and one a vasectomy. One of the operative procedures was a radical breast amputation.

In only one of these operative procedures, the prostatectomy, would one expect to have any postoperative bleeding. This fact accounts for the long delay in this particular case before a diagnosis of thrombocytopenia was made.

Four of these cases showed evidence of abnormal bleeding within three days; the remaining three bled seven to eight days. Bleeding into any postoperative wound is a serious complication and is occasionally seen. It must be ascertained that no bleeding vessel is present, and this fact can be promptly determined. In the absence of a bleeding vessel a thrombocytopenia must be ruled out.

Unfortunately, in unrecognized thrombocytopenias, preoperative platelet counts are not usually available. Consequently, a markedly decreased platelet count in the presence of clinical bleeding is the most useful aid in diagnosis. It would be desirable to have bone marrow evidence of megakaryocytic activity to substantiate the diagnosis; however, many times active bleeding necessitates immediate treatment.

Rarely the thrombocytopenia may be due to one of the blood dyscrasias, such as aplastic anemia, the leukemias, or splenic disorders causing thrombopenia other than essential thrombocytopenia. In general the clinical and laboratory examinations done in the routine preparation for surgery would reveal these diseases. The thrombocytopenia could certainly follow previous administration of toxic chemicals and drugs such as arsenicals, benzene, or possibly phenobarbital, quinine, or ergot. History in most instances will rule out this possibility. In the seven cases presented there was neither a history of medication nor any clinical or laboratory evidence of concomitant blood dyscrasia. In three of these cases bone marrow studies substantiated the clinical and laboratory diagnosis of thrombocytopenic purpura.

The exact method of treatment must be decided on the circumstances of the individual case. Certainly supportive therapy with repeated transfusions of fresh blood is of value. This permits the patient to improve by replacing the lost blood, and with a prompt disappearance of the thrombocytopenia improvement will follow.

Recent work has suggested a more definitive treatment by attempting to replace in the circulatory plasma an adequate amount of platelets to control the bleeding. Steafanini and Dameshek found the most effective way to administer platelets was the direct transfusion of polycythemic blood by multiple silicone-coated syringes. Somewhat less effective was the collection and administration of polycythemic blood in plastic silicone-treated sets.[6] Minor and Burnett transfused platelets separated from the normal blood and resuspended. They found that the method by which these platelets exerted their effect was unknown because the platelets disappeared promptly from the circulation. However, the improvement in bleeding tendency persisted several days beyond the time when the platelet count returned to its pretransfusion level.[4]

Moolten describes a substance, thrombocytosin, which is a lipoidal substance extracted from egg yolk and other fatty materials of animal origin. This is capable of elevating the platelet count and platelet adhesiveness, thereby inducing remissions in certain cases of thrombocytopenic purpura. This substance apparently acts as an antagonist of thrombocytopen, which is a lipoidal substance found in the spleen and has been indicted as the platelet-depressing agent.[5]

Welch and Dameshek have suggested that corticotropin (ACTH) and cortisone may be used in the treatment of acute thrombocytopenia.[7] Of 12 patients treated by Wilson, only 5 responded to corticotropin and cortisone. The effect of these substances is not at all clearcut, and Wilson also noted that the effect of the pituitary adrenal system on platelets has been observed experimentally. Bilateral adrenalectomy results in a rise in platelets, and animals which have been hypophysectomized have lower platelet counts. It is possible that corticotropin and cortisone affect an unknown immunothrombocytopenic mechanism.[8]

Postoperative wound hemorrhage due to thrombocytopenia may be treated conservatively with supportive therapy and repeated fresh blood transfusions if the bleeding is not severe. Cortisone and corticotropin may prove to be adjuncts in this treatment. If bleeding is severe and the safety of the patient is in danger, then an immediate splenectomy should be done. Hirsch and Dameshek feel that splenectomy performed during the acute fulminating course of a thrombocytopenic purpura carries an undue mortality.[8] Welch states that mortality during the acute crisis is from 24 to 30%.[7] Zollinger reports an over-all mortality from splenectomy of 5.5% and for primary hypersplenism of 1.1%.[10] We have had no mortality from splenectomy during the acute phase.

In the cases reported the patients were not in the classic acute fulminating phase, and undoubtedly in the absence of an operative procedure the thrombocytopenia would have gone unnoticed. Hence, since these cases probably represent the chronic type of thrombocytopenia, the operative risk is much less. Green and associates have suggested that all cases of thrombocytopenia should be prepared preoperatively with corticotropin. They feel that this may control the acute hemorrhagic phase of the disease and lessen the surgical risk.[2]

We did not use corticotropin or cortisone preoperatively in any of the four cases in which splenectomy was done. We experienced no technical difficulties and had no fatalities. It seems most logical to treat these bleeding postoperative cases with splenectomy, for conservative therapy in the presence of severe hemorrhage may result in a fatality.

SUMMARY

The problem of unrecognized thrombocytopenia in the presence of severe postoperative hemorrhage is presented.

Seven cases of unrecognized thrombocytopenia are presented, with charts showing the variations in the platelet counts.

Four of these cases were treated by splenectomy, two by repeated fresh blood transfusions and supportive therapy, and one by cortisone therapy.

Various types of available treatment are described and discussed, including fresh blood transfusions, platelet transfusions, and the use of thromybocytosin.

In this series, splenectomy was the treatment of choice for severe postoperative hemorrhage due to a previously unrecognized thrombocytopenia.

Drs. Robert M. Cochran and George N. Johnson permitted use of their cases, No. 3 and No. 4, respectively.

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MALIGNANT MELANOMA

Treatment and End-Results in Two Hundred and Twenty-Five Cases

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IT IS NOW generally appreciated that the treatment of operable malignant melanoma is surgical. However, there is still much uncertainty about some of the details of surgical treatment. For instance, when one excises a malignant melanoma, how wide should the excision be? Should one dissect the regional lymph nodes in all cases of melanoma of the skin or only in those cases in which the nodes seem to contain metastases? Should an amputation be done in preference to wide excision in treating melanoma of the extremities? In an attempt to crystallize our ideas regarding some of these questions, we have recently reviewed the cases seen at the Veterans Administration Hospital, Hines, Ill., prior to July, 1948.

MATERIAL STUDIED

The diagnosis of malignant melanoma was made in 294 cases between December, 1930, and July, 1948. However, material was available for microscopic study in only 248 of these cases. This tissue was reexamined microscopically, and the original diagnosis was not substantiated in 23. The remaining 225 cases form the basis of this study. Distribution of the primary lesions is given in Table 1. All patients were males. Ages at time of onset of the disease varied from 18 to 77 years. The diagnosis of juvenile melanoma was not made at Hines Hospital during this period. Nine patients were Negroes (4%). Of 41 patients with melanoma in the uveal tract, 1 was a Negro (2.4%), and of 164 patients with melanoma of the skin, 6 were Negroes (3.7%). Eight per cent of all patients admitted to Hines Hospital are Negroes. Melanoma in Negro patients most frequently involves the feet. Thus, 6 of 26 melanomas of the feet occurred in Negroes (23.1%), and 3 of 12 melanomas on the sole were seen in Negro patients (25%). Eleven of Bauer's[1] collected series of 14 cases of melanoma in the Negro occurred on the sole of the foot. More than one primary melanoma was seen in only one patient in this series.

Read at the 11th Annual Meeting of the Central Surgical Association, Detroit, Feb. 19, 1954.

From the Department of Surgery, Northwestern University Medical School, Chicago, and the Veterans Administration Hospital, Hines, Ill.

Dr. William L. McNamara, Chief of the Department of Pathology, reviewed many of the microscopic preparations of tissue from patients included in this study.

Mr. Phillip W. Zinkgraf, Chief Medical Statistician, and Miss Hazel Hanley, Director of the Tumor Registry, Hines Hospital, gave valuable help in the preparation of this paper.

FOLLOW-UP OF PATIENTS

All except 1 of the 225 patients were followed for more than five years or until death. Thus, follow-up data are complete in 224 patients treated prior to July, 1948, for calculation of 5-year survivals and in 154 of 156 patients (98.7%) treated prior to July, 1943, for calculation of 10-year survivals. In the calculation of end-results, patients lost to follow-up during the stated intervals and patients known to have died of causes other than melanoma were considered an indeterminate group and excluded from the calculation. Table 2 gives the survival according to the site of the primary lesion in terms of 5- and 10-year survival from time of onset and from time of treatment.

TREATMENT AND RESULTS

Most patients were in an advanced stage of the disease when admitted to Hines Hospital, and only palliative treatment was possible. Nine patients, 22% of those with melanoma of the eye, and 70 patients, 43% of those with melanoma of the skin

TABLE 1.—*Distribution of Lesions* *

Location	Patients					
	No.			%		
Eye	41			18.2		
Skin	164			72.9		
Trunk †		61			27.1	
Head and neck		33			14.7	
Extremities		70			31.1	
Upper			20			8.9
Lower			50			22.2
Mucous membrane	3			1.3		
Primary undetermined	17			7.6		
	225			100.0		

* This distribution includes all cases of malignant melanoma from December, 1930, to July, 1948.
† One patient with melanoma of the trunk developed a second primary malignant melanoma on a lower extremity.

were unsuitable for anything but palliative treatment, and the conditions of all patients with melanoma of mucous membrane or with the primary site undetermined were too advanced for definitive treatment on admission.

Melanoma of the Skin.—Radiation therapy was used as a definitive method of treatment in 23 operable patients in the early years covered by this study (prior to 1944). In two patients it was used to treat the primary lesion, without control of the neoplasm in either case, and in 21 cases it was used as treatment for metastatic melanoma in regional node areas after excision of the primary lesion. The metastatic disease was also uncontrolled in these patients. Of the total number of patients, 22 died of melanoma and 1 of other causes.

Because melanoma is a radioresistant tumor, surgery has been the treatment of choice since 1942. This has consisted of excision (usually wide) of the primary lesion or amputation for operable patients without clinical evidence of lymph node metastases. When regional nodes were involved, a regional lymphadenectomy (usually radical) was added. Table 3 gives the 5- and 10-year survivals. In the group of 33 patients treated by excision or amputation, there were 23% 5-year survivals and no 10-year survivals.

TABLE 2.—*Survival According to Site of Primary Lesion* *

Site of Primary Lesion	Total Cases Admitted Prior to July, 1948	Determinate Cases (Onset)	Lived 5 Yr. or More After Onset		Determinate Cases (Treatment)	Lived 5 Yr. or More After Initial Treatment		Total Cases Admitted Prior to July 1943	Determinate Cases (Onset)	Lived 5 Yr. or More After Onset		Determinate Cases (Treatment)	Lived 5 Yr. or More After Initial Treatment	
			No.	% Determinate Cases		No.	% Determinate Cases			No.	% Determinate Cases		No.	% Determinate Cases
Uveal tract	41	38	21	55.3	38	17	44.7	30	26	10	38.5	25	10	40
Skin	164	157	33	21.0	156	24	15.4	116	108	8	7.4	104	7	6.7
Head and neck	33	30	8	26.7	30	8	26.7	21	18	3	16.7	18	3	16.7
Trunk	61	57	10	17.5	57	7	12.3	45	41	3	7.3	39	2	5.1
Extremities	70	70	15	21.4	69	9	13.0	50	49	2	4.1	46	2	4.3
Upper	20	20	4	20.0	20	3	15.0	11	11	0	0	11	0	0
Lower	50	50	11	22.0	49	6	12.2	39	39	2	5.1	36	2	5.5
Mucous membrane	3	3	0	0	3	0	0	2	2	0	0	2	0	0
Primary undetermined	17	17	0	0	17	0	0	7	7	0	0	7	0	0
Total	225	215	54	25.1	214	40	18.7	155	143	18	12.6	138	17	12.3

* Includes all cases of malignant melanoma from December, 1930, to July, 1948.

Forty-seven determinate cases were treated by regional lymphadenectomy in addition to excision or amputation. On the basis of palpable lymphadenopathy or biopsy, these patients were thought to have nodal metastases. Microscopic examination of resected nodes confirmed the presence of metastases in all except one case. The 5- and 10-year survival rates in this group were 28 and 22% respectively.

Since regional lymphadenectomy was not employed in patients who had no clinical evidence of regional node metastases, it is of interest to determine the subsequent course of the disease and status of lymph nodes in these patients. Table 5 lists the

TABLE 3.—*Five- and Ten-Year Survival Rates* from Time of Initial Treatment (Melanoma of the Skin)*

Treatment at Hines Hospital	Total Cases Treated Prior to July, 1948	Determinate Cases	Lived 5 or More Yr. After Treatment		Total Cases Treated Prior to July, 1943	Determinate Cases	Lived 10 or More Yr. After Treatment	
			No.	%			No.	%
X-ray therapy to primary	2	1	0	0	2	1	0	0
X-ray therapy to involved nodes	21	21	0	0	20	20	0	0
Excision of primary or amputations †	33	30	7	23.3	18	15	0	0
Excision of primary or amputation and regional lymphadenectomy ‡	48	47	13	27.7	24	23	5	21.7
Palliative treatment only	70	68	0	0	40	38	0	0

* Eleven patients are listed twice. Five who had excision of a primary melanoma had x-ray therapy to regional lymph node metastases at a later date, and six, who had excision of a primary melanoma, had regional lymphadenectomy at a later date.

† No patient had clinical evidence of lymph node metastases at time of treatment.

‡ All except one patient had microscopically proved involved lymph nodes.

TABLE 4.—*Lymph Node Metastases by Sites (Malignant Melanoma)*

Location	Total Patients	Total with Metastases		Present on Admission		Developed After Admission		Not Stated	
		No.	%	No.	%	No.	%	No.	%
Eye	41	7	17.0	4	9.8	3	7.3	0	0.0
Skin	164	139	84.8	121	73.8	18	10.9	5	3.0
Head and neck	33	25	75.8	17	51.5	8	24.2	2	6.1
Trunk	61	54	88.5	49	80.3	5	8.2	0	0.0
Extremities	70	60	85.7	55	78.6	5	7.1	3	4.3
Upper	20	17	85.0	16	80.0	1	5.0	0	0.0
Lower	50	43	86.0	39	78.0	4	8.0	3	6.0
Mucous membrane	3	2	66.7	2	66.7	0	0.0	0	0.0
Primary undetermined	17	13	76.6	13	76.6	0	0.0	0	0.0
Total	225	161	71.5	140	62.2	21	9.3	5	2.2

number of patients according to the site of the primary lesion who had no clinical evidence of lymph node metastases on admission to the hospital. Of these patients, 8% with melanoma of the eye and 42% with melanoma of the skin subsequently were observed to have node metastases. These figures represent the minimum incidence of metastases in this group because some of these patients were followed only by letter, and the opportunity to examine the lymph nodes of some was therefore denied.

An explanation for the better results in the group of cutaneous melanoma in which dissections were done, as compared with the group in which they were not done, lies in the fallibility of clinical examination as a method of determining the

presence of lymph node metastases. In the 33 patients treated by excision or amputation, the lymph nodes were not considered involved by melanoma and therefore were not dissected. Fourteen (42%) of these were observed to have lymph node metastases at a later date.

This experience impressed us with the importance of the lymphatics in the dissemination of melanoma of the skin and has influenced us to undertake lymph node dissection in operable cases of cutaneous melanoma, regardless of the status of the nodes. The appearance of node metastases in 42% of patients who were without metastases on admission seems to us high enough to justify prophylactic lymphadenectomy.

Melanoma of the Uveal Tract.—In the determinate group there were 21 patients with malignant melanoma of the eye who received their initial treatment at Hines Hospital prior to July, 1948. One patient who had an advanced lesion was treated by exenteration of the orbit. Twenty patients were treated by enucleation of the

TABLE 5.—*Development of Lymph Node Metastases by Sites (Malignant Melanoma)*

	Patients Without Nodal Metastases on Admission *	Subsequently Developed Nodal Metastases	
		No.	%
Eye	37	3	8.1
Skin	43	18	41.9
Head and neck	16	8	50.0
Trunk	12	5	41.7
Extremities	15	5	33.3
Upper	4	1	20.0
Lower	11	4	36.4
Mucous membrane	1	0	0.0
Primary undetermined	4	0	0.0
Total	85	21	24.7

* Patients with clinical or microscopic evidence of nodal metastases on admission are excluded. Some of these patients had hematogenous metastases.

eyeball, 13 of whom (65%) survived the five-year interval. Among these patients, one local recurrence of melanoma in the orbit was observed (5%). Among 13 patients who had enucleation of the eyeball done elsewhere, four local recurrences (31%) were observed, making a total of five local recurrences (15%) among 33 patients treated by enucleation and observed for at least five years or until death. Thus, local recurrence can occasionally be expected after enucleation of the eyeball. There were no five-year survivors among patients who developed local recurrence. This raises the question of whether exenteration of the orbit might be preferable to enucleation for treatment of ocular melanoma and more in keeping with the principles of radical cancer surgery.

Lymph node metastases occurred only rarely in patients with melanoma of the uveal tract and were observed soon before death in seven patients. Two patients had cervical lymph node metastases and one developed axillary nodal metastases. In four patients mesenteric or hilar lymph node metastases were present at autopsy. The five patients who developed local recurrence in the orbit following enucleation succumbed to generalized metastases before cervical lymph node metastases were

observed. Thus, the regional lymph nodes are unimportant in the dissemination of melanoma of the uveal tract, and lymphadenectomy of cervical lymph nodes is not indicated.

FACTORS AFFECTING PROGNOSIS

Site of Primary Lesion.—Five- and ten-year survivals according to the site of the primary lesion are given in Table 2. The number of patients surviving melanoma of the eye is considerably higher than for melanoma arising elsewhere in the body. Thus 44.7% of patients with ocular melanoma were alive 5 years after treatment, and 40% were alive 10 years, as compared with 15.4% 5-year survival and 6.7% 10-year survival for melanoma of the skin. No patients with melanoma primary in mucous membrane or with the primary site undetermined survived the five-year interval. Pack [2] showed from a study of a larger series of cases that the highest incidence of survivals occurred with subungual melanomas and melanomas primary on the palm. In our series, one of five patients with subungual melanomas survived the five-year interval. Our only patient with melanoma of the palm died one year after onset.

Lymph Node Metastases.—Lymph node metastases were present on admission in 140 (62.2%) of the 225 patients and were observed to develop in an additional

TABLE 6.—*Relation of Lymph Node Metastases to Survival* *

Site of Lesion	Uveal Tract	Skin
Cases, no.	41	164
Patients with lymph node metastases on admission, %	9.8	73.3
Survived 5 yr. from onset, % of determinate cases	55.3	21.0
Survived 5 yr. from treatment, % determinate cases	44.7	15.4
Survived 10 yr. from onset, % of determinate cases	38.5	7.4
Survived 10 yr. from treatment, % determinate cases	40.0	6.7

* Includes all cases of malignant melanoma from December, 1930 to July, 1948.

21 (9.3%) after admission. Thus, a total of 161 (71.5%) patients were observed to have lymph node metastases at some time during the course of their illness. Table 6 contrasts certain clinical differences between melanoma of the uveal tract and melanoma of the skin, the most notable differences being the incidence of lymph node metastases and the differences in 5- and 10-year survivals. Lymph node metastases were present on admission in 4 of 41 patients with melanoma of the uveal tract (9.8%) and in 121 of 164 patients with melanoma of the skin (73.8%). The role of the lymphatic system in the dissemination of ocular and cutaneous melanoma may account for the difference in prognosis of melanoma primary in these sites. It is possible that if treatment of melanoma of the skin could successfully eradicate lymph node metastases that cutaneous melanoma would then have as good a prognosis as melanoma of the eye. This is a consideration which has influenced us to employ prophylactic regional lymphadenectomy for cutaneous melanoma.

Failure to Control the Primary Lesion.—Recurrence of the primary melanoma or persistence following initial treatment was observed in 58 patients (26% of the total). The primary lesion was inadequately controlled in 5 of 41 patients (12%) with melanoma of the uveal tract and in 51 of 164 patients (31%) with melanoma of the skin. Initial treatment in five recurrent cases of ocular melanoma

had been enucleation, four of which had been done elsewhere and one at Hines Hospital. Initial treatment of cutaneous melanomas in this group in most cases had been methods considered inadequate or even harmful. Many had been electrodessicated, fulgurated, treated with ointments and salves, x-rays or radium. Five recurrences were observed following excision of cutaneous melanomas at Hines Hospital, four of which did not have a sufficiently wide excision according to present standards. In two patients treated at Hines, both with melanomas of the scalp, attempts to excise the primary lesion were unsuccessful because of local extent of the lesions. These patients were inoperable. Although subsequent treatment was occasionally successful in controlling the primary lesion, only one patient with recurrent melanoma is still alive. The remaining 57 patients died with generalized metastases one month to four years after the recurrence was treated at Hines Hospital.

This experience emphasizes the importance of the initial treatment for malignant melanoma. When this treatment fails to control the primary lesion, the prognosis is indeed poor (2% of 58 determinate cases).

SUMMARY

Of 225 male patients with malignant melanoma observed between December, 1930, and July, 1948, there were 224 followed for at least five years or until death.

Lymph node metastases were observed in 17% of patients with melanoma primary in the uveal tract and in 84% of melanomas primary on the skin.

Forty-eight patients with cutaneous melanoma, 47 of whom had lymph node metastases, were treated by excision of the primary lesion and regional lymphadenectomy. The 5- and 10-year survival rates were 27.7 and 21.7%.

In a group of 33 cutaneous melanomas treated by excision of the primary lesion, regional lymphadenectomy was not done because of lack of clinical evidence of nodal metastases. The five-year survival rate in this group was 23.3%. There were no 10-year survivors.

Irradiation was used as a definitive method of therapy in 23 operable patients with cutaneous melanoma. The disease was uncontrolled in these patients, and there were no five-year survivals.

Treatment of operable cutaneous melanoma should be wide excision of the primary lesion or amputation and regional lymphadenectomy, regardless of lymph node involvement.

The importance of adequate initial treatment is emphasized. When initial treatment failed to control the primary lesion, the five-year survival rate was 2% (1 among 58 patients).

DISCUSSION

DR. R. K. GILCHRIST, Chicago: May I ask the essayist one question?

In a lesion on the foot or on the hand, did you do a block excision of the lymphatics all the way to the regional nodes, or not?

DR. FREDERICK W. PRESTON, Chicago: If the primary melanoma is on the foot or hand, we dissect the inguinal or axillary node areas but not the popliteal or cubital nodes. We do not do the dissection in continuity with removal of the primary lesion according to the method described by Pack.

There were 26 melanomas primary on the foot or ankle and 3 primary on the hand in this series of patients. In only one instance was growth of melanoma observed in the lymphatic channels between the primary and the inguinal or axillary nodes in these 29 patients. This patient had a melanoma primary on the heel with inguinal lymph node metastases. He also had metastases to the popliteal nodes. If this patient had been operable, a popliteal node dissection, in addition to a groin dissection, would have been done.

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RATIONALE OF INTERNAL MAMMARY LYMPH NODE DISSECTION FOR CARCINOMA OF THE BREAST

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HALSTED * laid the cornerstone for the effective treatment of carcinoma of the breast by stressing the importance of removal of the entire breast and overlying skin, the pectoral muscles with their fascial envelopment, and the regional lymphatics and lymph nodes. He recognized the supraclavicular extension from the axilla and included resection of the nodes in the latter area as a part of the radical operation in 101 cases included with his published report of 1907. He also predicted that in the future the removal of the mediastinal lymph nodes would probably become a part of the usual operative procedure. He apparently regarded the added operative trauma of the supraclavicular dissection as of questionable virtue, since only 2 of the 44 patients in whom the nodes were found to be involved were cured for five years or more. That fact probably discouraged extending the operation to include the mediastinal nodes, which he recognized as a significant part of the lymphatic drainage area of the breast.

W. S. Handley [3] recognized the significance of the internal mammary chain in breast carcinoma but recommended radium needle implantation in the intercostal spaces after unfavorable experiences with surgical removal of the nodes. His son, R. S. Handley,† carried forward the work of his father and advocated exploring the parasternal intercostal spaces as a diagnostic and prognostic procedure. The studies of Dahl-Iversen [5] and Soerenson [6] added greatly to the knowledge of lymphatic spread to the internal mammary chain. Haagenson and Stout [7] included in their criteria of inoperability involvement of the intercostal or parasternal nodes. McDonald, Haagenson, and Stout [8] reported their experiences with internal mammary node dissections. They described a "triple biopsy" procedure (primary lesion, internal mammary nodes, and supraclavicular nodes) and emphasized the high incidence of supraclavicular involvement when the internal mammary chain was involved (due to poor filtration of tumor cells by the small, often widely separated nodes of the internal mammary chain). If the internal mammary and supraclavicular nodes were not involved, radical mastectomy was performed at a second stage, or if the axillary nodes were not involved in certain medial quadrant tumors block resection of the parasternal area was done at a second stage. It was the contention of these authors that performance of the internal mammary exploration and supraclavicular biopsy

From the Division of Surgery, St. Luke's Hospital.

Read at the 11th Annual Meeting of the Central Surgical Association, Detroit, Feb. 19, 1954.

* References 1 and 2.

† References 4 and 5.

and the radical mastectomy in one stage involved an operative procedure of unjustifiable length. They have evaluated the possibilities in a scholarly and provocative manner.

Adair,[9] Gilchrist,[10] Orr,[11] and Wanke [12] have called attention to the potentialities of more radical breast surgery for carcinoma.

Urban,[13] Sugarbaker,[14] and Wangensteen ‡ in this country and Berri,[15] Brenier,[16] Detrie,[17] Mörl,[18] Margottini and Bucalosi,[19] Redon and Lacour,[20] and Tailhefer [21] on the continent have advocated massive resections of the breast, pectorals, axillary contents, chest wall, and internal mammary chain in continuity and, in some cases, supraclavicular nodes and substernal mediastinal nodes.

It seems pertinent to examine the rationale of an extended operation for breast carcinoma, with particular reference to the status of the internal mammary lymph nodes.

While it is impossible to compile conclusive statistical data concerning the frequency of internal mammary chain metastases from carcinoma of the breast, certain generalizations seem justified on the basis of available data from the literature § and my own experience. These generalizations may be stated as follows:

1. The axilla is the predominant site for lymph node metastases, regardless of the location of the primary carcinoma in the breast.

2. An occasional medial quadrant neoplasm will metastasize to the internal mammary chain only.

3. An axillary quadrant neoplasm rarely if ever metastasizes to the internal mammary chain alone.

4. The majority of internal mammary chain metastases occur when the axillary lymphatics are already blocked with tumor cells, and the medial quadrant neoplasm is the predominant source of the metastases.

5. Supraclavicular nodes are commonly involved also when the internal mammary chain contains metastases but infrequently when axillary nodes are involved without concomitant internal mammary metastases.

6. The finding of internal mammary metastases indicates a relatively poor prognosis.

The preferential route to the axillary lymphatics is readily demonstrated by the injection of visible dye into or about the tumor at the time of operation. When the axillary lymph nodes are uninvolved by tumor, the dye proceeds at once along the lymphatics leading to the axilla or infraclavicular nodes. When, on the other hand, the dye proceeds at once toward the internal mammary nodes, one may suspect that the axillary lymphatics are blocked by tumor cells.‖

It has seemed reasonable, therefore, to concentrate our efforts upon investigating the status of the internal mammary nodes and the effect of their involvement on prognosis in carcinoma of the breast medial to the areola. Believing that on the basis

‡ Wangensteen, O. H., cited by McDonald, Haagenson, and Stout.[8]

§ References 4, 5, 8, 16, 18, and 19.

‖ We have also used dye injections with the hope of aiding recognition of parasternal lymph nodes at the time of dissection, but we have found that, although the dye promptly reached the nodes, it often cannot be seen in the tiny nodes of this chain until they are transected. The procedure has not therefore aided in recognition of the nodes at the time of operation.

of present evidence massive resections of the chest wall or other procedures carrying a high morbidity and potentially crippling to the patient are unjustified, and believing that it would also be desirable to complete the definitive operation in one stage, if that is possible with safety, we have carried out the following procedure in a small group of cases of inner quadrant carcinomas which were clinically operable by the criteria of Haagenson and Stout.[7]

OPERATION

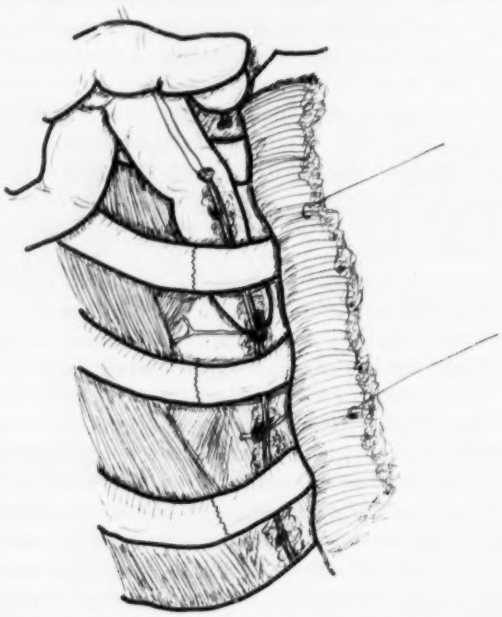
Employing a transverse perimammary incision (the location of the tumor determines whether a vertical or transverse incision is made), we divide the medial insertion of the pectoralis major vertically parallel to the margin of the sternum and about 3 cm. lateral to that margin. The medial portion of the muscle is reflected over the sternum, and the major portion of the muscle is reflected laterally. At this point a specimen is taken for biopsy from the primary lesion or the lesion is resected for frozen section. The external and internal intercostal muscles are then cleared from the first through the fourth intercostal space, adjacent to the sternal margin. Internal mammary vessels are identified at the lower margin of the first rib, usually about 1.5 cm. from the manubrium, where they lie on the fascia propria over the parietal pleura. By this time the frozen section has been completed and the diagnosis confirmed. The vessels are doubly ligated with 000 or 0000 silk and divided. The proximal stump immediately retracts beneath the first costal cartilage. The fat and fascia about the vessels are cleared from the parietal pleura without entering it. The ligature on the internal mammary pedicle distally is grasped between the operator's thumb and index finger, and the latter is insinuated between the first and second ribs, gently elevating the vessels from the pleura as they pass beneath the second costal cartilage. Vessels are dissected from the deep surface of the costal cartilage until the anastomosing branches of the intercostal artery are visualized, ligated, and severed (Figure). The same procedure is followed in the second, third and fourth interspaces and the entire chain of vessels, nodes and surrounding fat is removed in one piece. These are immediately sent to the laboratory for frozen section. With gentle dissection it is usually possible to remove the chain without tearing any of the branches. The index finger protects the pleura and also may be useful in compressing the artery against the costal cartilage in the event a ligature slips off or a branch is torn. Occasionally it is necessary to divide and elevate a cartilage if one of the anastomotic arteries tears off and retracts. Absolute hemostasis is, of course, essential in this area. The cuff of the pectoralis major that has been reflected over the sternum is then tacked down to the costal cartilages and remaining intercostal muscle fibers to obliterate partly the dead space between the cartilages.

To leave this margin of pectoral muscle is not ideal, but its presence is a distinct aid to wound healing.

If the frozen sections of the nodes are negative for neoplasm, the pectoral muscles and breast are reflected laterally and an axillary dissection is carried out. If the nodes contain carcinoma in the internal mammary chain, as shown by the frozen section, the breast and pectoralis major are turned back to expose the axilla and the axillary nodes are examined grossly. If they are obviously extensively involved, the operation is terminated and the breast and pectoralis major are resected, leaving the axillary flap undisturbed for external x-irradiation. If no obviously involved nodes are found in the axilla or only one or two in the inferior pectoral chain, the axillary dissection

is completed on the chance, which is admittedly slight, that the nodes in the internal mammary chain represent the only metastases present. It is our opinion that to do a block resection of the chest wall in such cases is futile, for if there has been retrograde extension along the lymphatic channels into the pleura or mediastinum or liver nothing is likely to be accomplished by a more radical procedure.

The combined procedure of internal mammary dissection and radical mastectomy has required from three hours in a very thin, elderly patient to five hours in an obese patient. The internal mammary portion of the dissection adds one and one-half to two hours to the time required for radical mastectomy. Wound healing has not been



Diagrammatic sketch of operative procedure for resection of internal mammary lymph nodes. The medial insertion of the pectoralis major muscle has been divided and reflected over the sternum. This is used to fill the intercostal spaces at completion of the dissection. The intercostal muscles have been cleared from the first four intercostal spaces. The internal mammary vessels have been divided beneath the first costal cartilage and the operator's index finger has been insinuated between the parietal pleura and the fascia propria, fat, and vascular components of the internal mammary chain until the anastomotic intercostal vessels have been ligated and interrupted. In the second interspace a dilated lymphatic channel may be seen on the parietal pleura, coursing toward an involved lymph node. This channel may be assumed to contain tumor cells when the lymph node is blocked with tumor.

significantly complicated by the intercostal dissection. There has usually been an accumulation of serum in one or more interspaces sufficient to necessitate aspiration and, in one instance, incision and drainage.

COMMENT

McDonald, Haagenson and Stout [8] have called attention to the poor filtering quality of the internal mammary nodes and the free anastomosis between the lymphatics of the first intercostal space with those of the opposite side, and to the short

distance between this interspace and the sentinel node at the confluence of the internal jugular and subclavian veins. We have observed on several occasions dilated lymphatic channels lying directly on the pleura leading directly to the node blocked with tumor cells and also dilated lymphatics leading beneath the sternum toward the mediastinum. It must be assumed that these dilated lymphatics may contain tumor cells in such circumstances. We have also demonstrated by anatomic dissection that there is considerable variation in the course of the internal mammary vessels. In one clinical case these vessels turned medially sharply in the third interspace, continuing their course deep to the sternum. All these observations would seem to militate against the effectiveness of any block resection of the chest wall which does not include resection of the sternum and the contralateral internal mammary chain. The latter procedure does not seem justified, and, even if accomplished, it would not eliminate retrograde metastases along the pleural lymphatics. It would seem more logical, therefore, to utilize the internal mammary dissection as a diagnostic and prognostic indication and not to include it as a part of a block resection expected to be curative.

During the past year we have employed the internal mammary dissection as described in eight cases of breast carcinoma distinctly medial to the areola. It would seem reasonable to treat similarly all central tumors as well. Adair [9] has suggested that the internal mammary chain dissection may prove to be advisable as a part of every radical mastectomy. We are not prepared to advocate the procedure for all operable breast carcinomas until more experience has been obtained with medial and central neoplasms.

Of the eight cases of medial quadrant breast carcinomas which form the basis for this report, all were solid, undifferentiated neoplasms, seven occurring in the right breast and one in the left. Axillary lymph nodes were involved in four cases, and of the four cases two had internal mammary metastases as well. In one of the latter, supraclavicular nodes were also involved. All four of the patients with axillary involvement received postoperative x-irradiation. In addition, the premenopausal cases, three in number (one without metastases), received x-ray therapy for castration. In none of the patients in this small group was convalescence significantly delayed by the internal mammary dissection. In only one instance was supplementary drainage of a serum collection in an intercostal space required. All the patients were free from recurrence or demonstrable remote metastases at the time of this report. In one case it was found impractical to dissect the fourth intercostal space because the lymph chain and artery turned abruptly beneath the sternum at the level of the fourth costal cartilage. In one case the first interspace was inaccessible because of overlapping of the first costal cartilage on the second.

Several observers have called attention to the insignificant size of the lymph nodes of the internal mammary chain when uninvolved with infection or neoplasm. The normal nodes are actually so small as often to be invisible. When they are clearly visible, the surgeon may expect them to contain tumor; when not visible they are not necessarily free of tumors. If the internal mammary chain is removed as part of a block resection including ribs, costal cartilages, and pleura, and the line of resection stops at the sternal margin, some of these tiny nodes may well be missed as they retract beneath the sternum, unless the surgeon be unusually wary. "Block resection" is a magic term in cancer surgery, but unless it combines finesse with force it may defeat its purpose.

SUMMARY AND CONCLUSIONS

It is concluded that internal mammary node dissection is useful primarily as a diagnostic and prognostic index preliminary to radical mastectomy for central and medial quadrant carcinomas.

A simple technique is described which it is believed may be carried out as an adjunct to radical mastectomy without significantly increasing the operative hazard.

It seems probable that most cases of breast carcinoma demonstrating involved internal mammary lymph nodes should be considered inoperable. It seems unlikely that either block resection or local excision of the nodes will be curative if these nodes contain tumor.

DISCUSSION

DR. R. K. GILCHRIST, Chicago: This is a very interesting subject, and one that may offer some real dividends in the future.

Within the past three or four weeks I heard Dr. Urban discuss his results. He has not had any cases that have gone five years as yet, and every patient that had involved nodes in this chain died of cancer, more or less bearing out Dr. Glover's story.

I am afraid that Dr. Glover's thesis is correct, that we really do not know just exactly where cancer spreads when it turns to the internal chain. Just how effective the filter action is around this group, how often the cancer jumps to the other areas, what skip areas there are, and so on, is very important.

If this group of surgeons would make a group effort to take the patients who died in the hospital after mastectomy, before their tumor had had a chance to spread, and would do a block clearing of all of the tissues that might contain lymphatic metastases, carefully drawn up the way we do it, for instance, in the bowel, remembering that about 0.5% of the patients who have a breast amputation die in the hospital, the pooling of such information over a period of two or three years would give us a very accurate picture of just what we are missing, and it would allow us to discuss such a paper with a good deal of decision and force.

As it is today, each of us has his own personal experience and impression about this matter, and we really don't know. I think that is the answer to Dr. Glover's story.

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ESOPHAGEAL REPLACEMENT WITH PLASTIC TUBES

Experimental Study

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ESOPHAGEAL replacement has been accomplished successfully by using autogenous tissues and plastic tubes. The goal of each of these procedures is to establish the continuity of the esophagus following a surgical resection.

The desirability of using the patient's own tissue for esophageal reconstruction is not questioned; however, each of the tissues used has limitations. Skin tubes not only require multiple procedures to develop an adequate blood supply but also lack peristaltic activity and frequently develop fistulae at the site of anastomosis. The stomach, although the logical and desirable organ to use for esophageal replacement, is at times not available because of previous disease and, on occasions, has proved to be of inadequate length to bridge the esophageal defect.

The experiences of Longmire and Ravitch [1] Shumacker and Battersby,[2] and others with the use of jejunum emphasizes the difficulty in mobilizing long lengths of jejunum and preserving an adequate blood supply for extensive esophageal replacement.

The colon has been used by Kergin,[3] Battersby,[4] and others as a means of esophageal replacement. Although this replacement can be accomplished in one stage, it is a procedure of considerable magnitude. Furthermore, the viability of the colon may be compromised by thrombosis of collateral vessels. We have used the right colon with success in six cases, but in one the interpolated segment was lost because of vascular thrombosis.

The objective with the use of plastic materials is an immediate restoration of the continuity of the esophagus by a well tolerated prosthetic device about which a new esophagus develops from the host's tissues. The use of semirigid polyethylene tubes as esophageal substitutes as suggested by Berman [5] has attained considerable success, although reported experiences indicate that difficulties may occur. Commercially available molded polyethylene tubes have two disadvantages. For one thing, these are available only in standard dimensions with regard to diameter and length. For another, the tubes can not be anchored in place by the usual methods of suturing.

From the Indiana University Medical Center.

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Read at the 11th Annual Meeting of the Central Surgical Association, Detroit, Feb. 19, 1954.

This paper reports preliminary observations with the use of a plastic tube for esophageal replacement so constructed that it can be inserted by the usual methods of suture anastomosis.

MATERIALS

Both polyethylene film and nylon cause a minimal response in tissue and, from this standpoint, are suitable for use in the experimental animal and the human subject.[6] Polyethylene film has the advantage of being impervious to water. It is of

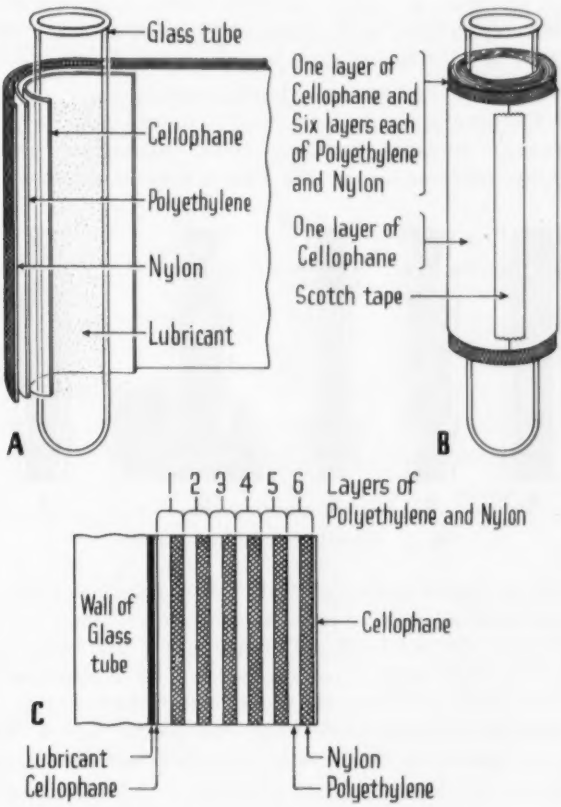

Fig. 1.—Diagram of plastic-tube construction.

inadequate tensile strength and rigidity unless it is used in considerable thickness. Nylon mesh, on the other hand, has considerable tensile strength with a minimum bulk, a lack of rigidity, and a high degree of porosity, depending upon the thread count per square inch. The use of polyethylene film and nylon mesh fused together as a laminated material was originated by one of us (H. K.) and has been studied and developed in the surgical laboratories as a material for bridging certain other tissue defects. As a laminated prosthetic device for esophageal replacement, it was found desirable to fuse several layers of nylon mesh and polyethylene film in order

to get the proper thickness and rigidity. The low melting point of polyethylene as compared with the higher melting point of nylon is utilized to fuse the layers of the tube together. The heat of an autoclave for sterilizing instruments is adequate to bring about fusion. When these materials are wrapped around a suitable mold and placed in the autoclave, a laminated plastic tube of any desired thickness, length, and flexibility can be made. A tube of this composition is thin-walled and has the texture and flexibility of polyethylene but the strength and durability of nylon.

The polyethylene film used was animal-tested and in sheet form, 0.002 in. thick.* The nylon used was from a standard source.† Fabrics with two different thread counts were used. Nylon fabric #241 contained 270 by 204 threads per square inch, while fabric #5051 had 188 by 182 threads per square inch.

A glass test tube of desired size proved to be a suitable mold. Figure 1 schematically indicates the manner in which the tube is formed prior to the curing and sterilizing process. A lubricant, hexachlorophene (pHisoHex), and Cellophane[7] are used as a protective cover for the tube while it is in the autoclave.

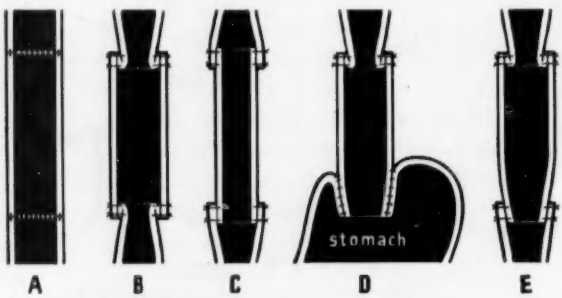

Fig. 2.—Method of suture anastomosis.

A plastic tube of desired quality with fabric #241 proved to be six layers thick, each layer being composed of one film of polyethylene and one thickness of nylon. With fabric #5051, which is a fabric with larger spaces and fewer threads, it was found desirable to use two sheets of polyethylene and one of nylon per layer; again, six layers proved to be a satisfactory thickness for the completed tube. These laminated plastic tubes are fused and sterilized only as they are needed. The tubes may be resterilized by autoclaving but become stiffer and less flexible, although still suitable for use.

The ends of the tubes are made several layers thinner to provide an end that is more flexible than the body of the tube. These more flexible ends make it possible to sew the tube in place without damaging it. A suitable method of uniting this plastic tube to the esophagus by a suture anastomosis was then sought.

EXPERIMENTAL DATA

Mongrel dogs of average size were used. Each animal had had food withheld 12 hours prior to surgery, with no other preparation. Basal anesthesia with intravenous pentobarbital (Nembutal) was supplemented by positive-pressure oxygen and ether administered through endotracheal

* Supplied by Clay-Adams Co., New York.

† Supplied by Stehli & Co., New York.

intubation. A standard thoracotomy incision was used to enter the chest through the fifth interspace. For the most part, a right thoracotomy was used. The esophagus below the level of the azygos vein was mobilized. Care was used to preserve the pleura of the mediastinum, although openings in the opposite leaf of pleura were common. A standard segment of esophagus of 4 to 6 cm. was excised between clamps. A plastic tube with a lumen equal to that of the esophagus was used. The postoperative care consisted of antibiotic therapy for a period of four to seven days, intravenous fluids for 24 hours, and resumption of liquids orally by the second day. A standard diet for laboratory animals was then used. The animals were observed for various periods of time. Esophagoscopy was performed on some animals in both the early and the late postoperative period.

Several different methods of inserting the graft (Fig. 2) were used to determine the most desirable way of uniting it to the esophagus.

TABLE 1.—*Results of Anastomosis*

Method	Dog No.	Results	Autopsy
A	#683*	Died 7 days	Sutures pulled out at both ends, graft lying free
	#685*	Died 7 days	.....
B	#690*	Living	.....
	#709*	Died 5 days	Distal leak, some necrosis
	#718	Died 6 days	Distal leak, short tube
C	#692	Died 1 mo.	Suture caused stricture, no leak
	#697*	Died 5 days	Leak (proximal)
	#742*	Died 5 days	Proximal leak
	#744	Died 3 days	Proximal leak
	#747	Living	.....
	#748	Died 1 wk.	Proximal leak
	#752	Living	.....
	#753	Died 15 days	No leak, atelectasis
E	#675*	Lived 2½ mo.	No cause found (see pathology sections)
	#689*	Living	.....
	#723*	Living	.....
	#725*	Living	.....
	#728*	Living	.....
	#738*	Died 6 days	Proximal leak (necrosis)
	#743	Died 8 days	Proximal leak
	#694	Died 7 days	Distal leak, tube too short
	#695	Died 8 days	Distal leak, tube too short

A review of each of the methods of uniting the graft not only contributed positive data but emphasized certain pitfalls that are to be avoided.

An end-to-end (Fig. 2*A*) union of the graft with the esophagus proved to be an unsatisfactory method (Table 1A). In each instance there was a disruption of both the proximal and the distal suture line before the process of healing became established.

The easiest method of inserting the graft is to place it inside the lumen of the esophagus and secure it by sutures to the cut end of the esophagus (Fig. 2*C*). This is essentially the method as described by Berman,[5] except for the method of suture. The data from this method (Table 1C) indicated a degree of success in reestablishing the continuity of the esophagus, although numerous failures were noted. There is a theoretical basis for objection to this type of union at the proximal end of the graft. Unless the graft fits firmly or is sewed tightly to the esophagus, there is the possibility that the caudal flow of food, fluid, or secretions might separate the proxi-

mal end of the graft from the esophagus. Should such a separation occur within the first week, a leak at the suture line could develop. Some of the data seemed to emphasize this point.

To overcome the theoretical objection of Method C (Fig. 2) a way of invaginating the esophagus into the graft was tried (Method B). This method overcame certain of the objections of Method C for the proximal end of the graft. However, Method B for the distal end of the graft merely created the disadvantages as recorded for the proximal end in Method C. In addition, the distal or second anastomosis was usually technically more difficult because of reduced mobility of the esophagus. The results of this type of anastomosis indicated only partial success (Table 1B).

Method D, although not entirely applicable to this study, did indicate a method of uniting the stomach to the graft. In each instance, the stomach was delivered into the chest sufficiently to minimize tension at the point of union with the graft.

In all of the experiments there was always an effort made to cover the graft as completely as possible with adjacent pleura.

TABLE 2.—*Failures of All Methods of Anastomosis Showing Location of Leak*

Method of Anastomosis	Dogs, No.	Failures, No.	Cause of Death	Location of Leak	
				Proximal End	Distal End
A	2	2	Leak	Both	
B	4	2	Leak	0	2
C	8	4	Leak	4	0
E	9	4	Leak	2	2 Short tube

A study of the failures associated with each of the methods used (Table 2) disclosed pertinent information about each. It is to be noted that the failures of Method C occur primarily at the proximal end of the graft. The failures of Method B were primarily at the distal end of the graft. Method A produced failures at both ends of the graft. The best procedure proved to be the use of Method C for the distal anastomosis and Method B for the proximal anastomosis. This procedure is illustrated in some detail in Figure 3. It should be noted that the proximal anastomosis is completed first, after which the distal anastomosis is completed without difficulty (Figs. 4 and 5). The data from a series of animals treated by this method are recorded in Table 1E. It is of interest that three of the operations were performed by other persons working in the laboratory and all ended fatally from leakage. Six operations were performed by us. Five were successful, and only one was a failure.

A review of the autopsy data from all of the methods studied indicated that failure could be attributed to necrosis at the suture line, the use of tubes that were too short, or faulty suture methods which did not produce a watertight union of the plastic tube with the esophagus. The healing process was demonstrated as complete at the end of two and one-half months by an autopsy of a killed animal (Fig. 6). A reconstructed esophagus with an adequate lumen and a thin wall was noted. The gross specimen (Fig. 7) demonstrated adequate continuity of the esophagus. Histologic study of the newly formed tissue tube demonstrated that complete epithelization had occurred (Fig. 8).

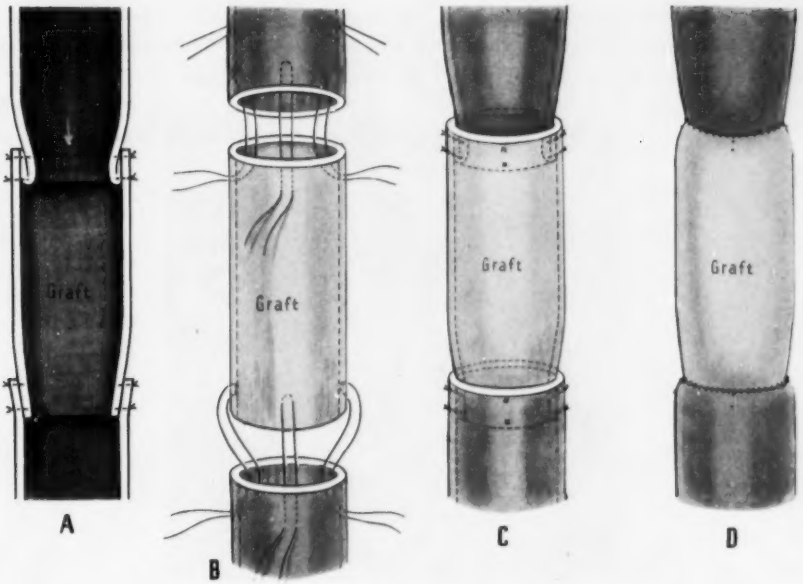

Fig. 3.—Details of inserting plastic tube into esophagus for Method E (Fig. 2).

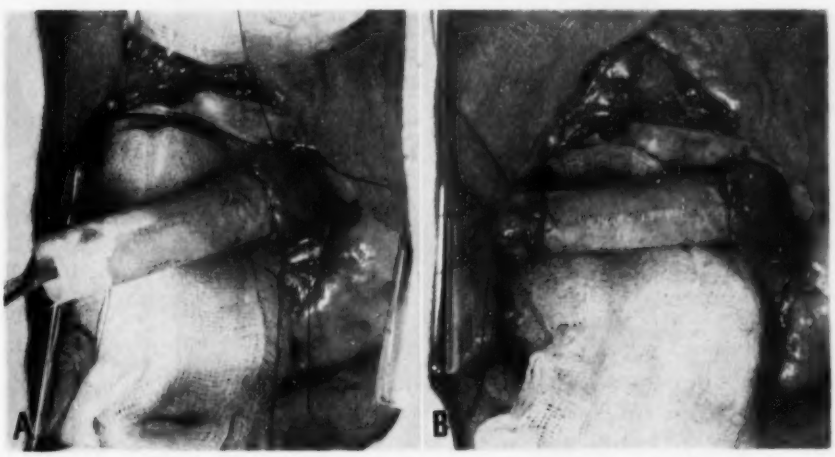

Fig. 4.—*A*, plastic tube inserted into proximal end of esophagus; *B*, plastic tube insertion completed.

Postoperative Observations.—The animals that survived the procedure experienced very little eating difficulty in the early postoperative period. Esophagoscopy was performed as early as the 14th postoperative day. In each instance the esophagoscope was passed down the esophagus past the graft and into the stomach without difficulty. The graft was observed to provide an adequate lumen for the esophagus.

Fig. 5.—Graft completely covered with pleura.

Fig. 6.—Autopsy picture demonstrating reconstruction segment of esophagus with adequate lumen.

A few animals experienced some eating difficulty at the end of three to four months' time. Esophagoscopy at this time did not disclose an obstruction at the area of excised segment of the esophagus. There was complete epithelization of the tissue tube; however, the plastic tube was completely detached from the esophagus.

Fig. 7.—Picture of gross specimen demonstrating complete healing.

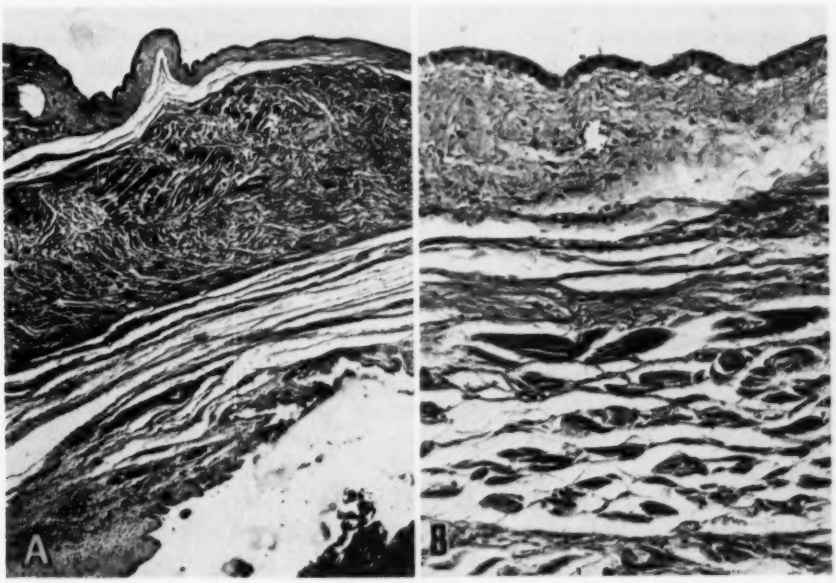

Fig. 8.—Photomicrographs. Note complete epithelization, both low- and high-power view.

COMMENT

There are certain points of interest that need emphasis. From a review of the autopsies on the animals that died as a result of a leak at the anastomosis, it was quite apparent that the success of the procedure depends upon the immediate watertight union of the plastic tube to the esophagus. This anastomosis must then remain watertight until a membrane composed of fibrin and pleura is formed about the prosthesis. A suitable union of the graft with the esophagus is established only for a period of four to seven days. By the end of this time, the sutures have usually cut out of the esophagus. The continuity of the esophagus is then maintained only by this newly formed tube of tissue about the graft. The process of healing then progresses to the point of complete epithelization of this newly formed tissue tube. In the late postoperative period the plastic tube probably ceases to serve a useful purpose and then acts as a foreign body. The prosthesis should probably be removed then.

It is equally important to emphasize that the plastic tube must be of adequate length to permit suture to the esophagus without tension. The tube must be equal to the length of the replaced segment of esophagus plus the amount necessary to provide a 1.5 cm. cuff at each end and also be long enough to allow for the distance that the esophagus retracts after it is severed.

Certain of the failures in all methods studied were due to a devascularization of the ends of the esophagus by an overzealous mobilization of this organ or the use of constricting suture material. This is a hazard not peculiar to this type of esophageal replacement but to esophageal surgery in general. It is apparent that the better results obtained in this study were by persons thoroughly familiar with esophageal surgery.

From a study of the healing process it is apparent that the plastic tube should be covered with adjacent tissue, as the success of the procedure is largely dependent upon the early formation of a tissue tube to restore esophageal continuity.

Even though the immediate results are promising for the preferred method of anastomosis, further study is in progress to determine when the prosthesis ceases to serve a useful purpose. Likewise, additional observations of possible late complications, such as stricture formation or functional disturbance of the reconstructed segment of esophagus, are in progress.

SUMMARY

A method is described of forming a laminated nylon-polyethylene plastic tube that can be sutured.

A suitable method of inserting this tube by suture anastomosis is described.

Restoration of esophageal continuity depends upon the plastic tube serving as a prosthesis about which an epithelial-lined tube from the host's tissues can form.

ADDENDUM

This procedure has been used on six patients by us and by other persons. In five patients the tube has functioned well; however, in one patient, the tube acted as a foreign body and had to be removed.

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ANALGESIA FOR CHRONIC PAIN WITHOUT RESPIRATORY DEPRESSION

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REPORTED in this study, in which the drugs used were levorphan tartrate (levo-3-hydroxy-N-methylmorphinan tartrate dihydrate) and levallorphan tartrate (3-hydroxy-N-allylmorphinan tartrate), are the methods used in and the results of a survey to determine the dosage ratio of levorphan to levallorphan necessary to secure satisfactory analgesia with minimal respiratory embarrassment (Fig. 1). The inquiry was limited to patients with reasonably constant chronic pain who required narcotics. A total of 18 patients meeting these qualifications were studied (Table 1).

PROCEDURE OF INVESTIGATION

All observations were made by a single observer (C. C. S.). The 18 patients included both men and women, with ages ranging from 34 to 73 years. The severity of pain was graded as follows: 1, for mild pain; 2, for moderate pain; 3, for very uncomfortable pain, and 4, for very severe pain. In a preliminary interview with each patient preceding the application of the drugs, the reason for and the method of investigation were explained. Preliminary data including severity of pain, respiratory rate, and minute volume of respiration were recorded to serve as "control" values. Orders were written to discontinue all previous medication of narcotics, barbiturates, or sedatives and for the attending nurses to prevent the use of drugs other than those under investigation. The levorphan or its combination with the antagonist was prepared in aqueous solution and was administered by either the subcutaneous or the intravenous route at three-hour intervals as necessary. Careful observations as to the severity of pain at the time of administration, dosages of each drug, route and time of administration, degree and onset of satisfactory analgesia, and respiratory rate and minute volume were all recorded on a prepared case report form provided for each patient during the course of the investigation. The measurement of the severity of pain and degree of analgesia obtained was based upon the patient's own interpretation and evaluation. The grading of the degree of analgesia was as follows: 0, for no or equivocal analgesia; 1, for slight but definite analgesia; 2, for moderate analgesia; 3, for good analgesia, and 4, for complete analgesia. The respiratory minute volume was measured by means of a ventigrator.[9]

The 18 patients were divided into three groups. In the first group, consisting of seven patients, each patient was given 2 mg. of levorphan tartrate subcutaneously for a period of not less than 24 hours. This initial dose was increased to 4 mg. for an additional 24 hours for those patients in whom the 2 mg. dose was unsatisfactory. With each administration of levorphan tartrate a separate placebo of saline was also injected. After establishment of the optimum dosage requirement of levorphan tartrate on the basis of satisfaction on the part of the patient, the next step taken was the administration of narcotic and antagonist subcutaneously and simultane-

Read at the 11th Annual Meeting of the Central Surgical Association, Detroit, Feb. 19, 1954.

From the Divison of Anesthesiology, Department of Surgery, State University of Iowa College of Medicine.

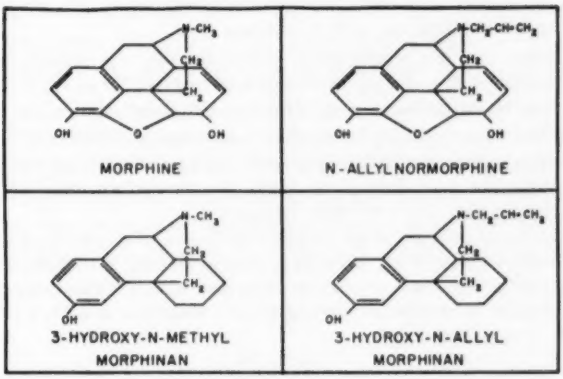

Figure 1

TABLE 1.—*Case Material*

Patients, No.	Diagnosis	Average Pain, Grade *
11	Carcinoma	2.6
1	Tic douloureux	3.0
1	Periarteritis nodosa with gangrene	3.0
1	Traumatic foot amputation	3.0
1	Tabes dorsalis	3.5
1	Sciatica	3.2
2	Pain of undetermined etiology	3.3
18	Total	Group average 2.8
	11 Men	7 Women
	Age range: 34-73	Average age: 53.3

* Grades are described in text.

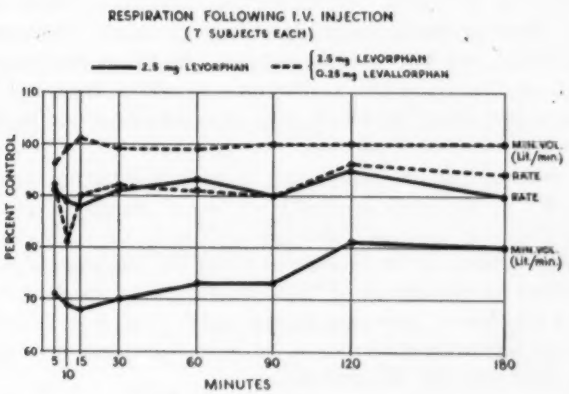

Figure 2

ously, but separately. The initial dosage ratio was four parts of narcotic to one part of antagonist. However, because of undesirable reactions, including loss of pain relief experienced by almost all the patients in this group, an 8:1 ratio was used.

A 10:1 ratio was tried in a second group, of four patients. For purposes of convenience of calculation, a combination dose of 5 mg. of levorphan tartrate and 0.5 mg. of levallorphan tartrate was employed. The two drugs were given subcutaneously simultaneously, but separately, as in the first group. This dosage combination provided a good degree of analgesia with a satisfactory degree of protection against respiratory depression. After application of the drugs simultaneously, but separately, the same doses in the same ratio were administered subcutaneously and simultaneously, but together from the same syringe.

To provide additional evidence of the adequacy of protection afforded by the antagonist drug when premixed with narcotic, 5 mg. doses of levorphan tartrate were given alone by the subcutaneous route and 2.5 mg. doses were given intravenously to a third group, of seven patients. Later, the same dosages of narcotic were premixed with antagonist in a 10:1 ratio and given by the same routes.

RESULTS

It is obvious from the data that levorphan tartrate and levallorphan tartrate in a 4:1 ratio resulted in a loss of analgesia. In addition, many of the patients to whom these drugs were administered in this ratio complained of nausea, extreme nervousness and restlessness, palpitation, cold sweats, hallucinations, and intensification of the original pain. These symptoms closely approximate the acute "abstinence syndrome" observed by Wikler and associates in patients addicted to morphine, methadone hydrochloride, or diacetyl-morphine (heroin) to whom they had administered N-allyl normorphine. These symptoms were apparently provoked by the antagonist after only one previous dose of narcotic.[10]

TABLE 2.—*Analgesia*

Drugs					
Levorphan Tartrate, Mg.	Levallorphan Tartrate, Mg.	Drug Ratio	No. of Cases	No. of Doses (Subcut.)	Average Analgesia per Dose (1-5 Hr.)
2	...	...	7	46	2.8
2	0.5	4:1	2	11	0.8
4	...	...	6	37	3.4
4	1.0	4:1	6	22	0.4
4	0.5	8:1	4	15	3.3
5	...	...	7	22	3.3*
5	0.5	10:1	11	82	3.5*

* No significant difference between these figures.

The data indicate that the combination of levorphan tartrate and levallorphan tartrate in an 8:1 or 10:1 ratio resulted in no loss of analgesia over that produced by levorphan alone. In addition, there appeared to be no significant evidence of reactions as experienced by the patients receiving the combination in a 4:1 ratio. Statistical analysis by the method of "Student's" t test of the data on the patients receiving the 5 mg. dose of levorphan tartrate and 0.5 mg. dose of levallorphan tartrate revealed no significant difference in the average analgesia per dose with levorphan tartrate alone and with the combination.

The interesting feature in the data on patients receiving 5 mg. of levorphan tartrate alone or in combination with 0.5 mg. of levallorphan tartrate is that statistical analysis reveals that there is no significant difference between the rates of respira-

tion in these two groups. However, there is a significant (p-0.1%) difference between the minute volumes of respiration. It is evident that the antagonist appears to prevent depression of respiration when used in combination with narcotic. The data are not unequivocally conclusive, because the circumstances of the clinical investigation made it difficult to secure random samples. In addition, objective measurements of minute volume were not made on all patients after they had received each dose of either narcotic alone or combination of narcotic and antagonist. As a result, it is possible that there was not a consistent depression of minute volume with each similar dose of narcotic alone. In this respect the investigation is incomplete. However, similar studies are in progress on additional patients, and a full-scale investigation of the effects of narcotic and combination of narcotic and antagonist on postoperative pain is planned.

TABLE 3.—*Respiration*

Drugs					Average Respiration, % of Control	
Levorphan Tartrate, Mg.	Levallorphan Tartrate, Mg.	Drug Ratio	No. of Cases	No. of Doses (Subcut.)	Rate	Min. Vol.
4	...	...	6	7	..	80
4	1.0	4:1	4	4	..	100
4	0.5	8:1	3	3	..	95
5	...	...	7	7	87*	71†
5	0.5	10:1	10	16	93*	98†

* No significant difference between these figures.
† Significant difference between these figures.

The administration of the pre-mixed solution of narcotic and its antagonist did not produce pain at the site of injection, either subcutaneously or intravenously. In some patients the narcotic drug provoked nausea and vomiting. This was not prevented or relieved by the administration of antagonist. All the 18 patients studied experienced a desire to sleep.

CONCLUSION

The data to date indicate that there is a ratio of narcotic and antagonist that will achieve analgesia without respiratory depression. With the opiate alone there is demonstrable respiratory depression; with excess antagonist in relation to narcotic, there are undersirable effects from the antagonist, such as symptoms similar to those of withdrawal.

Both narcotic and antagonist can be administered simultaneously, either subcutaneously or intravenously, in a pre-mixed solution. In suitable doses and in appropriate ratio, they can provide analgesia without respiratory depression.

The levorphan and levallorphan used in this study were provided by Hoffmann-La Roche, Inc., Nutley, N. J.

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CHEMICAL STERILIZATION OF ARTERIAL HOMOGRAFTS

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DETROIT

THE USEFULNESS of homografts for bridging arterial defects has been demonstrated in laboratory animals and after operations in humans.* In general, these grafts are functional after weeks or even months of storage if they have been removed aseptically and have been preserved in suitable solutions at low temperature. Naturally, there is no problem in obtaining adequate homograft material for animal experimentation, but it has been difficult to obtain sterile arterial segments from human cases. It would be advantageous if specimens removed at routine autopsies (and consequently unsterile) could be rendered sterile by a chemical process which would not denature the tissue in such a way as to compromise the results of grafting.

The common antibiotics and the sulfonamides are usually added to the solutions in which the grafts are preserved. However, these drugs do not always sterilize grossly contaminated specimens, and there also remains the remote possibility of virus, yeast, or fungus contamination. An agent lethal to all microbiological forms which would not harm the blood-vessel graft would be ideal. High-voltage cathode-ray irradiation was used by Meeker and Gross,[4] who found that a dose of between 2,000,000 and 2,500,000 rep appeared to give satisfactory sterilization with very little tissue damage. However, it was necessary to quick-freeze the specimens to prevent a reaction which generally caused thrombosis in the grafts. There were a few instances of infection apparently arising from the use of infected grafts in experimental animals. Most importantly, the method is practicable in only a few centers where such special irradiation equipment is available.

At the suggestion of Dr. Frank W. Hartman, we have investigated the action of two chemical agents, diacetylethylene (3-hexene-2, 5-dione) and beta-propiolactone. These had been studied as possible virucidal agents for the sterilization of plasma, and it had been demonstrated that they are lethal to bacteria as well as to viruses.†

Drs. James E. Cousar III and Thomas Geoghegan gave assistance.
This study was supported by a grant from the Michigan Heart Association.
From the Departments of Surgery and Laboratories of the Henry Ford Hospital.
Read at the 11th Annual Meeting of the Central Surgical Association, Detroit, Feb. 19, 1954.
* References 1 to 3.
† References 5 and 6.

EXPERIMENTS WITH DIACETYLETHYLENE

Diacetylethylene (DAE) is a white crystalline solid, slightly soluble in water, which is prepared by the dehydrogenation of acetonyl acetone. Its chemical structure is represented by the formula $CH_3COHC:CHOCCH_3$.

Arterial homografts for treatment with the agent were obtained as follows: Using unsterile technique, we removed the entire aorta from each of 11 donor dogs within one hour of death. The intercostal and abdominal arterial branches were ligated with silk. Each specimen was immediately placed in a flask containing 90 cc. of modified Tyrode's solution and 10 cc. of homologous serum.[7] The hydrogen ion concentration of the solution was then adjusted to pH 7.4 to 7.6 with sodium bicarbonate solution. The mixture was then inoculated with 1 cc. each of broth cultures of viridans streptococci and Staphylococcus aureus. The contaminated specimen was kept for 24 hours at 4 C. and bacterial counts made. DAE was then added to the flask at a concentration of 1 mg. per cubic centimeter of solution, and the specimen was refrigerated. Twenty-four hours later, bacterial counts were again made, and the pH was adjusted between 7.4 and 7.6. At appropriate intervals (Table 1), segments measuring approximately 1.5 cm. in length were cut off and implanted as grafts to bridge defects in the abdominal aortas of recipient dogs. The

TABLE 1.—*Results with Grafts Treated with Diacetylethylene*

Storage Interval, Days	Dogs, No.	Fatal Hemorrhage	Late Thrombosis	Calcification	Intimal Ulceration
2- 5	9	9	—	—	—
6-14	9	2	3	0	2
15-28	11	2	2	3	0
30-90	12	0	3	2	0

suture material was 5-0 Deknatel braided silk, placed as a continuous horizontal mattress suture with eversion of the vessel edges so that there was intima-to-intima coaptation. The animals that died during the early part of the experimental period were autopsied promptly, and the surviving animals were killed at intervals of two to eight months after implantation.

Results.—In no instance was a positive culture obtained from an aortic specimen 24 hours after treatment with DAE. Subsequent cultures were occasionally positive for nonpathogenic contaminants, such as Bacillus subtilis, but the original contaminating organisms were not recovered. Furthermore, there was no instance of infection about the graft in the 41 animals.

The fate of the implanted grafts is shown in Table 1. The most striking fact is that when the grafts were implanted early (i. e., within 5 days of the treatment with DAE), there was a mortality of 100% as a result of hemorrhage at the suture lines (Fig. 1). The incidence of this complication was lessened when the grafts were stored for longer periods, and after one month of storage, no deaths occurred from hemorrhage. However, the survival of the animals in the latter groups did not indicate function of the grafts, since 25% of them developed thrombosis and complete occlusion of the aorta at the site of grafting (Fig. 2*A*). This is a much higher incidence of thrombosis than we (Table 2) and others ‡ have encountered in

‡ References 2 and 3.

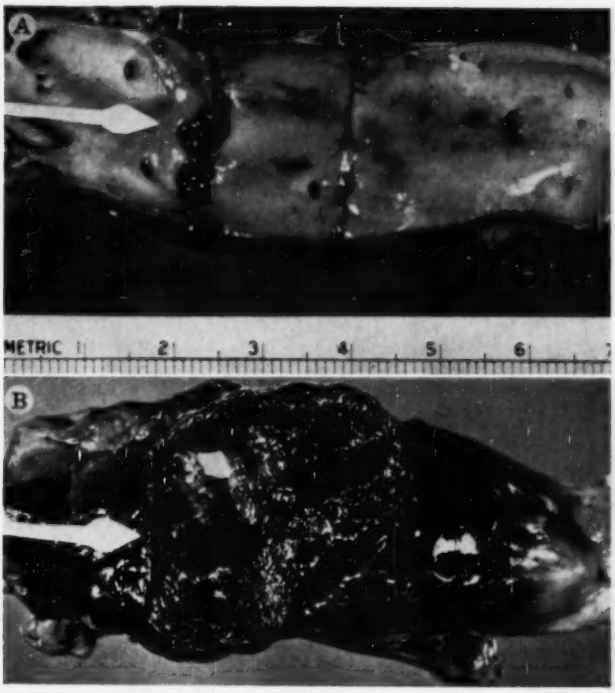

Fig. 1.—Disruption of suture line and fatal hemorrhage on 14th day following use of arterial homograft treated with diacetylethylene and stored for seven days: *A*, intimal surface; *B*, external surface.

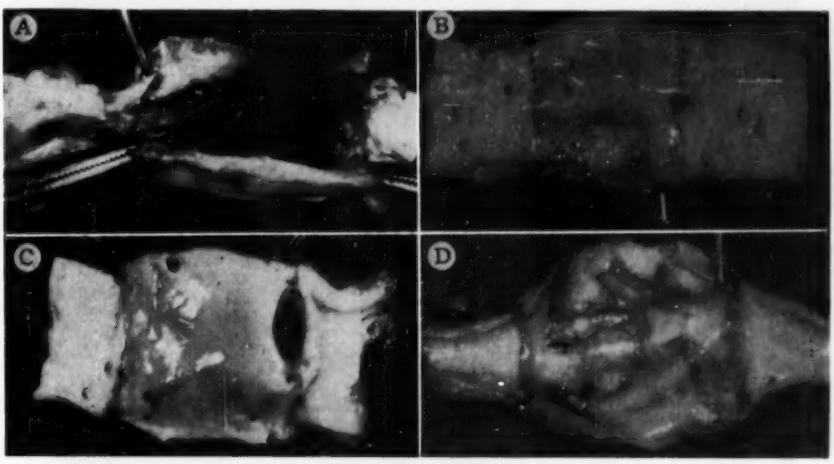

Fig. 2.—Late pathologic changes noted in grafts treated with diacetylethylene: *A*, thrombosis with complete occlusion in graft stored for 34 days; animal killed 70 days after operation; *B*, intimal ulceration in graft stored for 14 days; animal killed at seven months; *C*, nonfatal disruption of suture line with false aneurysm; graft stored for 43 days; killed at 60 days, and *D*, extensive calcification and dilatation of graft; stored for 27 days, killed at eight months.

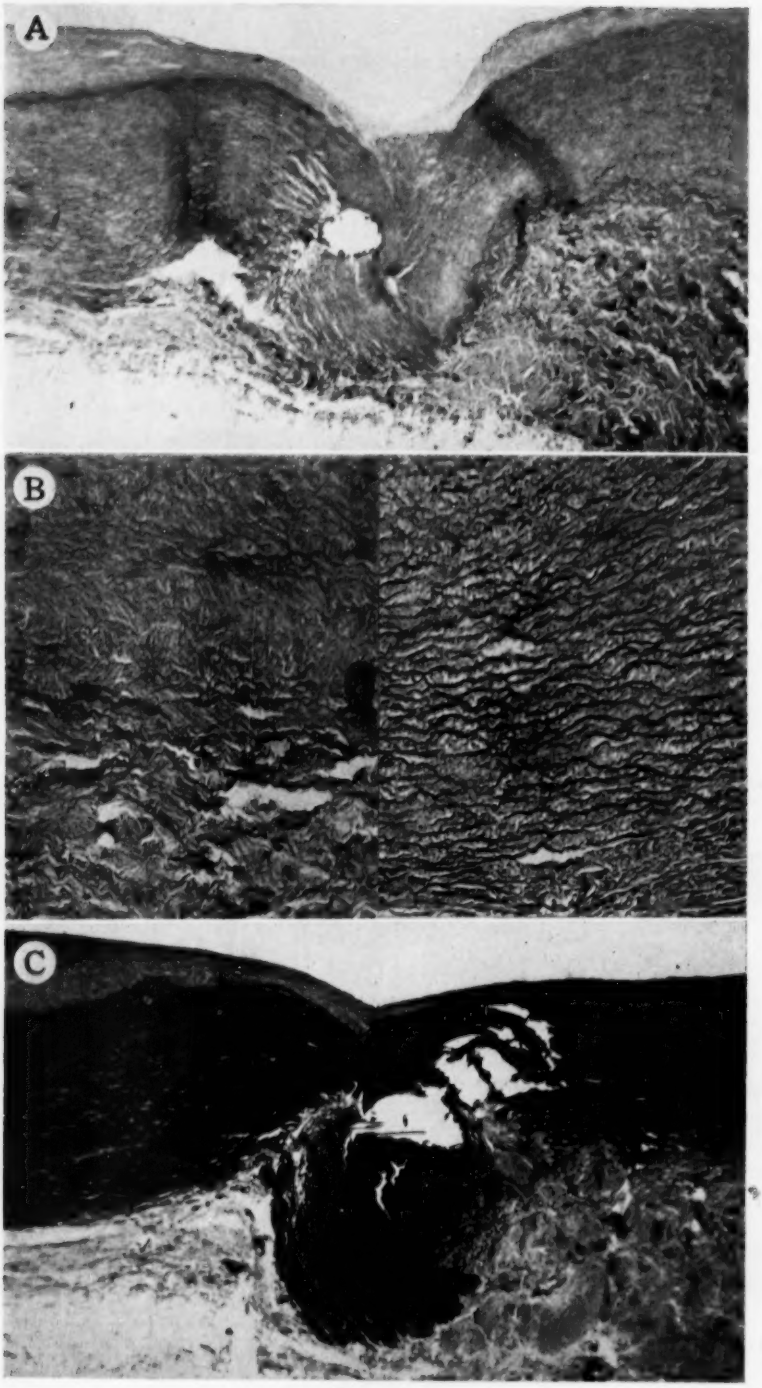

Figure 3

(See legends on opposite page)

grafts not treated with a strong sterilizing agent. Furthermore a number of functioning grafts showed degenerative changes, such as intimal ulceration and extensive calcification (Fig. 2 *B* and *D*). Representative specimens were studied histologically and showed a variety of pathologic changes in the grafts, corresponding to the gross appearance. The loss of cellularity of the media, common in all blood-vessel grafts, was especially striking (Fig. 3).

Conclusions.—Although diacetylethylene is an effective bactericidal agent, it is not practical for the sterilization of arterial homografts. If the grafts are used within five days of treatment with DAE, death of the animal from breakdown of the suture lines is to be expected. In grafts preserved for a longer period after treatment, there is an unacceptable incidence of thrombosis and degenerative changes.

EXPERIMENTS WITH BETA-PROPIOLACTONE

Beta-propiolactone (BPL),§ $H_2C\text{-}CH_2\text{-}C{=}O$ (O), is a viscous liquid with a specific gravity of 1.149, water-soluble to the extent of 37% by volume at 25 C. It is the simplest of the group of chemicals known as beta-lactones. It reacts with hydroxyl, amino, carboxyl, sulfhydryl, and phenolic groups, all of which are associated with proteins, but is stable in concentrated form for as long as 10 months when stored in the refrigerator in sealed ampules. A discussion of other chemical properties of the agent may be found in the studies of Gresham and others.[8]

The method of treatment of the grafts in the beta-propiolactone series differed in some respects from that in the diacetylethylene series. In order to obtain sterile controls, aseptic technique was used during the removal of the complete aortas from nine donor dogs. The aortas were divided into segments measuring 2 cm. in length, which were placed in flasks containing modified Tyrode's solution with 10% homologous serum, as in the first series. Half of the specimens were kept as untreated sterile controls and stored at 4 C. until time for implantation. The other specimens were contaminated with approximately 1,000,000 organisms per cubic centimeter of solution, obtained from 24-hour cultures of Escherichia coli and Aerobacter aerogenes. Approximately 1,000,000 desiccated Bacillus globigii spores per cubic centimeter of solution were also added. Beta-propiolactone was then added to obtain a concentration of 1% (weight/volume), and the mixture was incubated at 37 C. for two hours, after which bacterial counts were made. No viable organisms were recovered after treatment with BPL. The grafts were then removed from the mixture and stored in sterile modified Tyrode's solution at 4 C. for varying periods before implantation into recipient animals.

§ The beta-propiolactone was obtained from Dr. T. L. Gresham, B. F. Goodrich Research Center, Breckville, Ohio.

EXPLANATION OF FIGURE 3

Fig. 3.—Photomicrographs of suture line of specimen shown in Fig. 2*C*: *A*, hematoxylin and eosin stain, × 22; graft is on the left. *B*, higher magnification (× 140) of media of graft (left) and host aorta (right). The loss of cellular structure in the graft is striking. *C*, elastica trichrome stain of same section (× 22).

Results.—The fate of the control grafts may be seen in Table 2. Among the 15 controls, there were two instances of early death from hemorrhage at suture lines. No late thromboses were noted when the animals were killed nine months or more after the operation. One graft showed a small area of calcification.

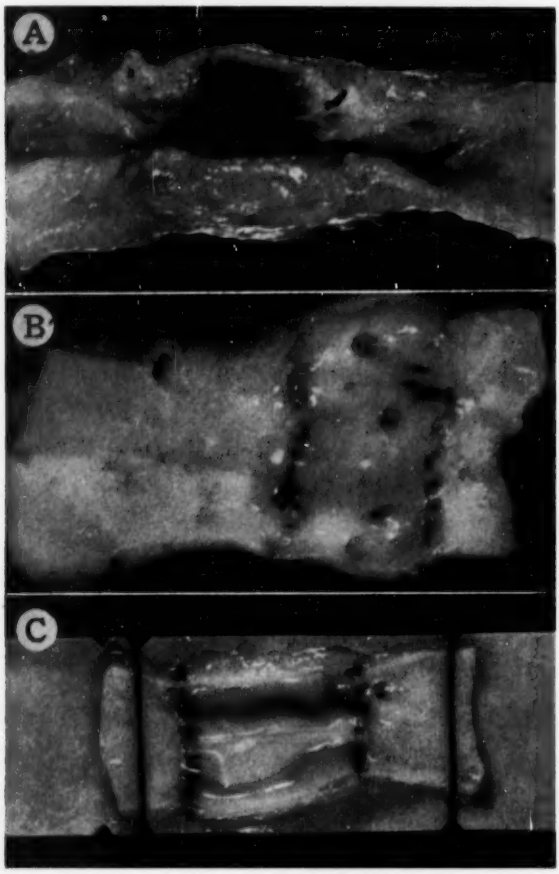

Fig. 4.—Examples of end-results in arterial grafts sterilized with beta-propiolactone: *A*, thrombosis and complete occlusion occurring in graft stored for four days; animal killed after 81 days. *B*, graft with excellent appearance. Stored 6 days; animal killed after 70 days. *C*, graft stored 6 days; animal killed after 647 days. Graft is perfect except for a tiny calcified plaque.

TABLE 2.—*Results with Sterile Control Grafts*

Storage Interval, Days	Dogs, No.	Fatal Hemorrhage	Late Thrombosis	Calcification	Intimal Ulceration
2- 5	5	0	0	0	1
6-14	5	0	0	0	0
15-28	4	2	0	0	0
30-90	1	0	0	0	0

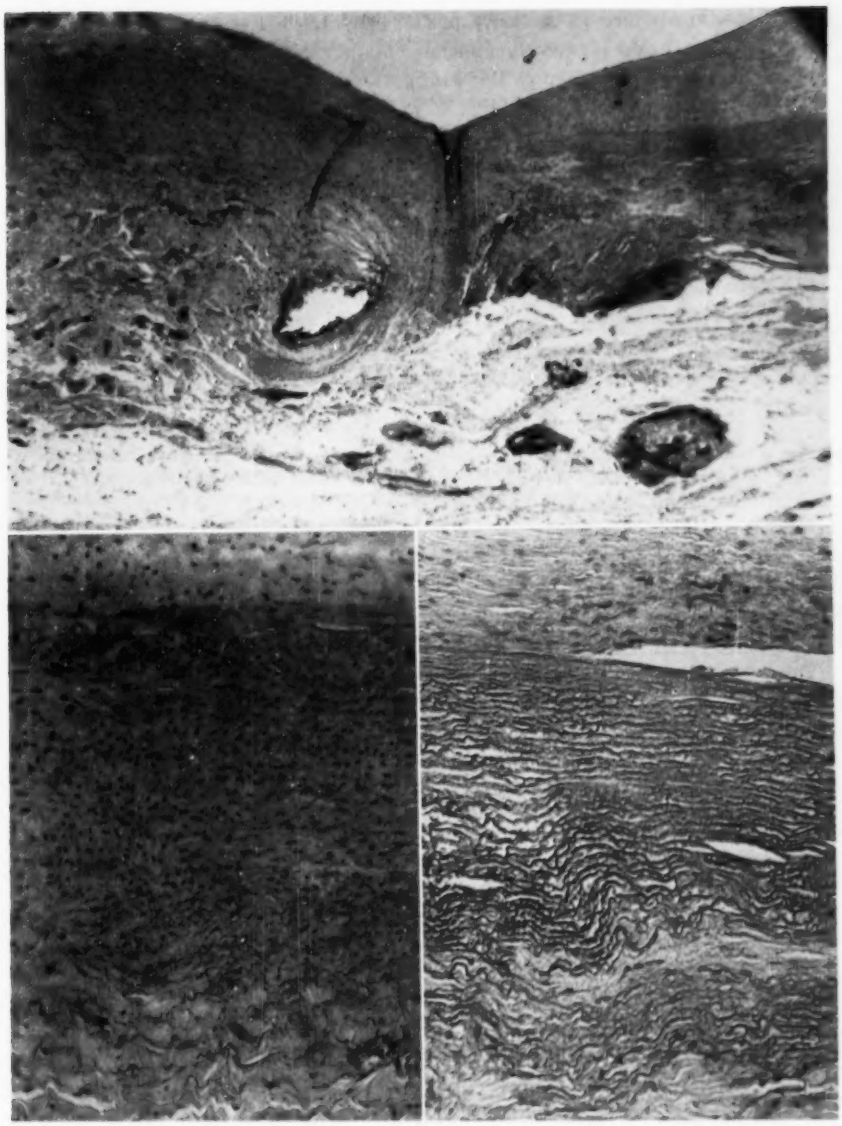

Fig. 5.—Photomicrographs of suture line of graft sterilized with beta-propiolactone and stored for four days before implantation. Killed 91 days later. Upper section, hematoxylin and eosin stain (× 22); graft is on the right. Lower sections, higher magnification (× 140) of host aorta (left) and graft (right).

Among the grafts treated with beta-propiolactone (Table 3), there was no instance of fatal hemorrhage and only one instance of thrombosis (Fig. 4*A*). Four of the 15 animals died in the early postoperative period of causes apparently not related to the grafts (extensive pneumonia in two, intussusception in one, no obvious cause in one). Ten of the survivors were killed after three months, and the other after almost two years (Fig. 4*C*). With the exception of a few tiny intimal ulcerations, the grafts appeared to be in excellent condition. Histologic study showed that the grafts did not differ significantly from the picture ordinarily seen when sterile, untreated grafts are implanted (Fig. 5).

CONCLUSIONS

Arterial homografts can be sterilized with the agent diacetylethylene, but there is an unacceptable incidence of early and late complications after implantation.

The compound beta-propiolactone effectively sterilizes the grafts and minimal adverse effects on the grafts have been apparent. Cautious clinical trial of this method of sterilization seems justified.

TABLE 3.—*Results with Grafts Treated with Beta-propiolactone*

Storage Interval, Days	Dogs, No.	Fatal Hemorrhage	Late Thrombosis	Calcification	Intimal Ulceration
2- 5	5**	0	1	0	1
6-14	5*	0	0	0	2
15-28	4*	0	0	0	1
30-90	1	0	0	0	0

* Indicates deaths in early postoperative period from unrelated causes. Each asterisk represents one death.

DISCUSSION

DR. D. E. SZILAGYI, Detroit: About two years ago at the Henry Ford Hospital we began to make plans for establishing a vascular bank; we soon found that it was impossible to obtain human vascular grafts with an aseptic technique and at the same time keep the good will of the pathologist. The preparation for and the actual performance of such operations are very time-consuming and may hold up an autopsy for several hours.

Therefore, we were exceedingly interested in the work that Drs. Trafas, Lo Grippo, and Lam were carrying on in dogs. About six months ago, Dr. Paul Overhulse, my associate, began to investigate the effects of a 1% beta-propiolactone solution by simple immersion for two hours on the histological structure, tensile strength, bursting strength, and tissue-culture viability of human grafts obtained at routine autopsies. He found that there were no significant deleterious effects. During the past four months we utilized beta-propiolactone-treated grafts in clinical cases. The lesions and the grafts were as follows: one case of aortic aneurysm with replacement of the bifurcation, one case of Leriche's syndrome with replacement of the aortic bifurcation, and six cases of superficial femoral arterial occlusion with replacement grafts varying in size from 8 to 28 cm. Of these cases, four have been too recent for angiographic studies (less than four weeks after operation). In five cases angiographic follow-up showed four to have remained in very satisfactory condition and one to have become occluded. This occlusion very likely was due to a technical error. The more recent cases present clinical evidences (such as oscillometer readings) of good function.

With your permission, I should like to show four slides of two cases.

[Slide] This is a case of occlusion of the superficial femoral artery in a man aged 54 with rather severe crural claudication.

[Slide] Here is the graft. The slight contour irregularities denote the ligatures on some of the arterial branches.

[Slide] This is a case of chronic thrombosis of the bifurcation of the aorta, or Leriche's disease; it is, as you will notice, fairly advanced.

[Slide] This shows the graft about five weeks after operation.

Our experience, of course, is very short-lived, the oldest case being only four months old; but, taken together with the animal experiments which have now extended over two years, and with the experimental work on human grafts formerly mentioned, we believe these results will probably stand the test of time.

Dr. John H. Grindlay, Rochester, Minn.: We learn a great deal and receive much help from our professional colleagues who are specialists in a field other than surgery. Dr. Heilman, head of bacteriology at the Mayo Clinic, some time ago suggested that the method we had been using in experimental and clinical studies with homografts for implantation in the aorta had a theoretical objection in that penicillin was supposed to inhibit bacterial growth.

He made the point that one minute after death there is an immediate invasion of the blood stream by bacteria from the intestines. He did not think that penicillin was the right material to employ to inhibit growth in the graft while it was being preserved, because the penicillin activity decreased. While it was active, it would only repress the growth of the bacteria which were sensitive, and all bacteria against which it was not effective would overgrow.

Therefore, he suggested that we use 1:1000 thimerosal (Merthiolate) solution, and it turned out that that was effective in all of our experimental grafts in preventing contamination; that is, at the time the grafts were implanted they were sterile, as they had been when they were cultured at the time of removal.

However, when the grafts were purposely contaminated with bacterial cultures, as was done in this study, the thimerosal was not effective.

Dr. G. A. Lo Grippo, Detroit: This is the chemical structure of beta-propiolactone, $H_2C\text{-}CH_2\text{-}C{=}O$ (the carbonyl oxygen closing the ring), a very unique compound which has been sitting on the shelves of the organic chemists since 1915. It came to us through a routine screening program in searching for an agent we could use for the sterilization of plasma.

Beta-propiolactone is unique in that it hydrolyzes very rapidly to nontoxic compounds, although it itself is quite toxic. It splits on either side of the oxygen ring and attaches to all the free-reacting groups of protein material. The degradation products from this compound are relatively nontoxic in the concentrations that are necessary to give us not only bactericidal but also fungicidal, viricidal, and sporicidal effects.

Beta-propiolactone must be carefully handled because it hydrolyzes so rapidly in water and more rapidly when proteins are present, although in its concentrated form it is very stable. By submerging it in ice water, hydrolysis can be kept at a minimum for an hour, but at 37 C. it hydrolyses rapidly, its half-life is approximately 30 to 45 minutes. Because it is toxic you must allow at least two hours at 37 C. for the compound to deteriorate.

The compounds formed after hydrolysis are very acid, but the fact that beta-propiolactone is viricidal and bactericidal in the pH range of 5 to 9 gives you a wide latitude. However, the solution must be continually neutralized, otherwise the pH will fall to an unsatisfactory low level. The final pH of the solution after BPL hydrolysis is dependent on a number of factors. We believe it is advisable to neutralize the acid products with 0.2 molar sodium bicarbonate (1.68 gm. per 100 ml. of solution), with phenol red (5 mg. per 100 ml. of solution) being used as an indicator.

Drug concentrations of this compound required to inactivate the microbiological forms vary. Viruses are inactivated in concentrations of 0.05 to 0.3%, and the fungicidal concentration is within 0.2 to 0.5%. Spores are the most difficult to inactivate, and we purposely used desiccated Bacillus globigii spores in this experiment, as the desiccated state is the most resistant. Five-tenths to 0.7% is necessary for sporicidal effect. However we used 1% beta-propiolactone for the sterilization of arterial grafts to assure a wide margin of safety.

The fact that the degradation products of beta-propiolactone are not bactericidal or viricidal makes it necessary to use the antibiotics to suppress further contamination. The main purpose here is initially to sterilize arteriografts and then maintain them under sterile conditions from then on.

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PSEUDOCYST OF THE PANCREAS: DIAGNOSIS AND THERAPY

Report of Ten Cases Treated by Transcystogastrostomy

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ST. LOUIS

MUCH OF the existing confusion regarding proper therapeutic measures for the treatment of cystic lesions of the pancreas stems from a lack of appreciation of the variety of cystic lesions which occur in the pancreas and the proper treatment of each type. In the last several years a number of reports have appeared, evaluating various forms of surgical treatment of pancreatic cysts. At the present time the use of internal drainage is receiving particular attention. In general, three types of procedure have been employed: cystogastrostomy, cystocholecystostomy, and cystojejunostomy. Some surgeons have used a Roux-Y jejunal limb in performing the latter procedure.[1] Up to the present time, a total of only 50 cases utilizing cystogastrostomy has been reported.[2] The present series of 10 cases * represents the largest single series reported to date and affords further material for evaluating this form of therapy.

The present report also contains a brief résumé of my personal experience with diseases of the pancreas at the Jewish Hospital as they relate to the present subject.

INCIDENCE OF PSEUDOCYST

From the data in Table 1, it is apparent that pseudocysts accounted for only 1.4% of the 370 cases of pancreatic disease diagnosed either clinically or at autopsy at the Jewish Hospital of St. Louis during an 18-year period. Of further interest is the frequency of other lesions of the pancreas which may resemble pseudocyst clinically. Twenty-four of the cases in the inflammatory group can be considered space-consuming lesions of sufficient size to warrant differentiation from pseudocyst as well as from neoplastic disease; this constitutes 6.6% of the 370 cases. Surprisingly, non-neoplastic cystic lesions of the pancreas occurred with over twice the frequency of neoplastic cystic disease. Particularly noteworthy is the small number of cases of pseudocyst in relation to the larger number of cases of acute and chronic recurring pancreatitis.

Read at the 11th Annual Meeting of the Central Surgical Association, Detroit, Feb. 20, 1954.

This investigation was supported by the David May-Florence G. May Research Fund of the Jewish Hospital.

From the Divisions of Surgery, The Jewish Hospital of St. Louis, and Washington University School of Medicine.

* Dr. H. Haffner, Dr. E. Bricker, Dr. S. Schneider and Dr. R. Elman contributed several of the cases included in this series.

CLINICAL ASPECTS OF TEN CASES OF PSEUDOCYST

Despite the fact that pseudocyst is a rare complication of pancreatitis, as shown in the previous section, all 10 patients in this series gave a history of previous repeated attacks of acute abdominal pain, and in 7 of these serum diastase determinations were performed. The values ranged from 1,100 to 6,800 Somogyi units. Acute abdominal pain was the chief complaint in every case at the time the cyst was dis-

TABLE 1.—*Comparative Frequency of Various Diseases of the Pancreas*

Disease	Cases	
	No.	%
Inflammatory		
Acute pancreatitis (proved)	199	53.8
Chronic or recurrent pancreatitis	40	10.8
Retention cyst	8	2.4
Abscess	7	1.9
Pseudocyst	5	1.4
Fistula	4	1.1
Congenital fibrocystic disease	4	1.1
Total inflammatory	267	72.5
Neoplastic		
Solid carcinoma	81	21.9
Cystadenocarcinoma	3	0.8
Cystadenoma	6	1.6
Lymphosarcoma	3	0.8
Islet cell adenoma	9	2.4
Lymphangioma	1	0.3
Total neoplastic	103	27.8
Total cases	370	

TABLE 2.—*Clinical Characteristics of Ten Cases of Pseudocyst*

	Category	Cases, No.
1.	Race { White	6
	Race { Negro	4
2.	Sex { Male	8
	Sex { Female	2
3.	Past history of one or more attacks of acute abdominal pain	10
4.	Elevated serum diastase with previous acute abdominal pain	7 (1,100-6,800 Somogyi units)
5.	Acute abdominal pain at time cyst was discovered	10
6.	Palpable abdominal mass	10
7.	Serum diastase taken at time of admission for transgastric cystogastrostomy	5 (224-300 Somogyi units)

covered, and in each of these patients there was a palpable abdominal mass. Serum diastase determinations were recorded in only five cases at the time of discovery of the cyst, and they ranged between 224 and 300 Somogyi units. On the other hand, diastase values of the cyst fluid obtained in three cases showed values in excess of 1,000 units.

It is apparent from these observations that a previous history pointing to acute pancreatitis is common in patients with pseudocyst. The cyst may be discovered by abdominal palpation of a mass and the presence of a moderately elevated serum diastase. The latter may indicate low-grade persistent disease of the pancreas or merely slow absorption of diastase through the cyst wall.

THERAPY

It is generally accepted that cysts of the pancreas call for surgical intervention. Conservative therapy may result in rupture. In the instance of neoplastic cyst, withholding surgery may lead to the spread of the tumor, and in the case of pseudocyst there may be rupture into the peritoneal cavity, with hemorrhage, shock, or peritonitis. According to Koucky, Beck and Todd,[3] rupture of a cyst carries a mortality of 60%.

Four forms of surgical treatment have been employed for pancreatic cysts: (1) marsupialization (external drainage), (2) excision, (3) partial pancreatectomy, and (4) internal drainage into the stomach, jejunum, or gall bladder.

1. Marsupialization has the disadvantage of complications such as persistent fistula, premature closure of a sinus tract with reformation of the cyst, excoriation of the skin, and, when a true cyst is present, a residual of malignant or potentially malignant tissue.

2. Excision is the treatment of choice for neoplastic cysts. However, it should be kept in mind that according to Kunc [4] there is a 10.7% mortality with excision of all cysts of the pancreas, which rises to 55.5% if the intended extirpation proved impractical at operation. This is particularly important when a pseudocyst is mistakenly taken to be a neoplastic one because of the absence of a cleavage plane in the former.

3. Partial pancreatectomy should be carried out for multiple small cysts whether inflammatory or neoplastic.

4. Internal drainage appears to be a most desirable method for treating pseudocysts, since it offers adequate drainage without the complication of persistent fistula or excoriation of the skin. Further, it has the advantage of simplicity as compared with the Roux-Y jejunal limb. The objection raised that the reflux of gastric juice into the cyst may cause digestion of the wall has not materialized in the cases previously reported or in the present series. However, Kafka [5] has observed a single case of hemorrhage following transgastric cystogastrostomy, and Maxeiner [6] has reported the development of a bleeding peptic ulcer at the anastomotic site.

Transgastric Cystogastrostomy: Isolated reports of successful internal drainage by primary anastomosis of the cyst to various portions of the gastrointestinal tract and the gall bladder have appeared in the literature since about 1927 (Hahn,[7] Walzel,[8] and Kirschner [9]). However, in the initial reports the mortality appeared to be higher than with marsupialization, owing to leakage of the anastomosis and peritonitis and, in some instances, to secondary infection of the cyst.

Transgastric anastomosis of a cyst was first reported by Jedlicka [10] in 1923 and by Jurasz [11] in 1929. Subsequent case reports have increased the number of cases so treated to 50 (Brandenburg, Maddock, and Schweitzer [12]; Kunc [4]; Scovel and Hollinger [13]; Zaoussis [2]). The present series raises the number of cases reported to 60. On one of his trips to Europe, Dr. Elman visited the Jurasz Clinic and on his return suggested that this procedure be tried.

One prerequisite for carrying out this procedure is that the cyst be at least partly retrogastric and adherent to the wall of the stomach. Most pseudocysts will meet this requirement. The abdomen is explored through a midline vertical incision, and

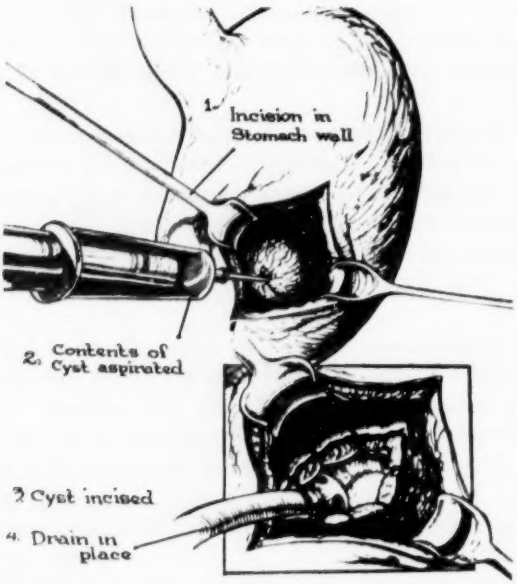


Fig. 1.—Figure shows various phases of the operative procedure, including the use of a catheter as employed in the early cases.

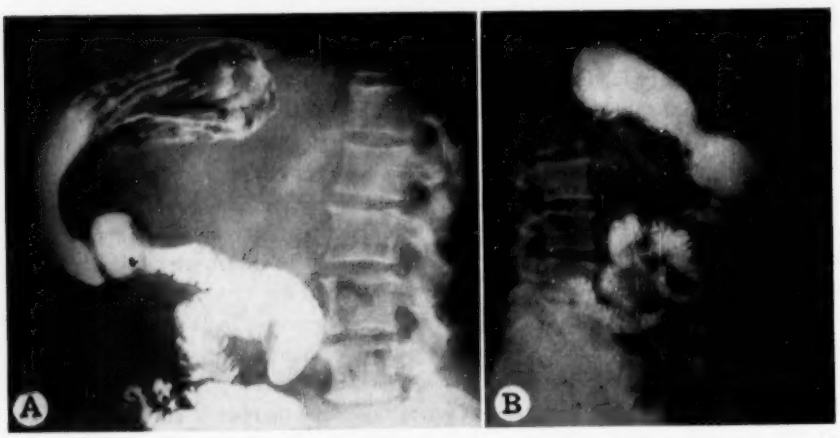
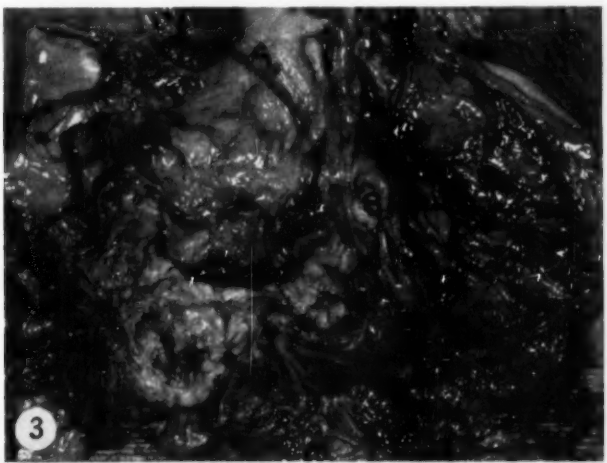


Fig. 2.—*a*, Lateral view showing distortion of posterior wall of the stomach by pressure from the cyst; *b*, Same patient two weeks later, showing return of stomach to almost normal shape following cystogastrostomy.

the liver, gall bladder, and head of the pancreas are examined. An incision is made through the anterior wall of the stomach and the cyst then aspirated (Fig. 1). A longitudinal incision about 1 to 2 in. (2.5 to 5 cm.) in length is then made through the posterior wall of the stomach into the cyst. The latter is explored with a finger



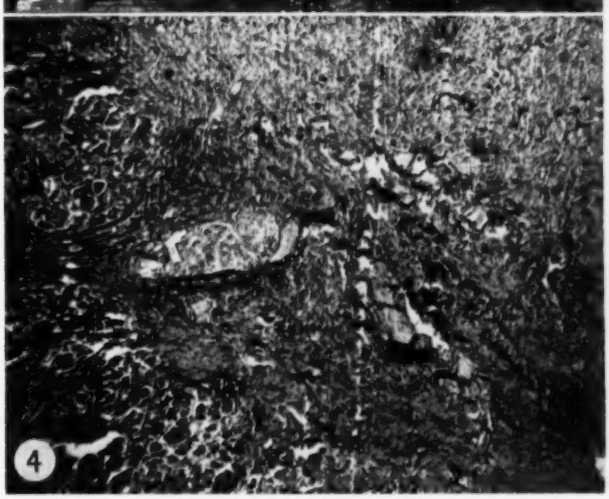


Fig. 3.—Gross specimen of stomach and pancreas removed at postmortem examination from patient who died six months after cystogastrostomy. The cyst area has been replaced by dense gray fibrous tissue; all that remains of the cyst cavity is a narrow tract containing a probe (*A*). Under *B* is a tiny opening in the gastric mucosa which communicated with the tract at *A*.

Fig. 4.—Microscopic section through the cyst area showing replacement of cyst cavity by dense collagenous fibrous tissue. Pancreatic parenchyma is present along the left margin.

and a biopsy specimen obtained from the wall for pathological examination. Multiple interrupted absorbable (gut) sutures are then placed circumferentially, as shown in Fig. 1, for hemostasis and to evert the gastric mucosa. In the first few operations

of this type, a large Pessar catheter was placed in the cyst cavity and brought out through the stomach and the anterior abdominal wall. Subsequent experience proved this step unnecessary. I now close the anterior wall of the stomach and the abdominal wound completely.

Postoperative evaluation. It is still somewhat premature to attempt a full evaluation of this method of treatment of pseudocysts of the pancreas. Four of the present cases have now gone over 20 months without recurrence, one for over 3 years, and another for almost 4 years. In none of the cases has there been a recurrence of symptoms.

One case is worth special attention. This patient, a 67-year-old man, presented a typical clinical situation of pancreatic cyst, as noted previously. In addition, a lateral view of the stomach following a barium meal showed a typical x-ray deformity of the stomach, which disappeared almost completely after transgastric cystogastrostomy (Fig. 2). During the following six months he appeared completely free of any complaints referable to pancreas or gastrointestinal tract. He died suddenly, and postmortem examination revealed a pulmonary embolism with infarction as a complication of hypertensive cardiovascular disease. During this six month period the cyst had been almost completely obliterated, autopsy revealing a thick fibrous mass, in the center of which there was only a narrow channel which communicated with the stomach through a tiny opening (Fig. 3). Microscopic section showed replacement of the cyst by dense collagenous fibrous tissue (Fig. 4). It appears, therefore, that a period in excess of six months is necessary for complete obliteration of the cyst and its artificial communication with the stomach but during this period there are no symptoms of pancreatic disease.

CONCLUSIONS

The present report brings to 60 the number of cases of pancreatic pseudocyst treated by transgastric cystogastrostomy. In all the cases in the present series there was at least suggestive evidence of previous attacks of acute pancreatitis, and in seven this was supported by markedly elevated serum diastase levels.

Further, the present report has not dealt in detail with the problem of differential diagnosis of cystic lesions and the relation of the latter to the choice of surgical procedure. In the final analysis this rests with the pathological diagnosis. The pathogenic and pathological aspects of cystic lesions of the pancreas will be dealt with in a subsequent study. However, I recommend the use of frozen section to rule out neoplastic cystic disease before proceeding with transgastric cystogastrostomy, and I shall continue to use this method of transgastric drainage until contraindicated.

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OPERATIVE CHOLANGIOGRAPHY AS AN AID IN SURGERY FOR JAUNDICE

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OPERATIVE or immediate cholangiography may be of great assistance to the surgeon who is dealing with a jaundiced patient. The cholangiogram may be of direct assistance by demonstrating the exact location and character of an obstruction. It may be equally useful in showing a completely normal extrahepatic bile duct system and thus help the surgeon prove that the jaundice is of hepatic origin.

A number of techniques for obtaining satisfactory operative cholangiograms are available, and each surgeon is likely to develop his own variations of the basic pattern. Of fundamental importance is close teamwork between the surgeon, roentgenologist, and anesthetist, and each of these must be aware of the problems of the other two. The equipment itself may be very simple. The x-rays used to illustrate this report were made with a standard portable x-ray unit, a Bucky frame, and a standard operating table. Before the operation the Bucky frame was placed on the operating table at the desired position and the table "built up" with blankets and mattresses to compensate for the thickness of the Bucky frame and permit the patient to lie level. The contrast medium employed was iodopyracet (Diodrast) or acetrizoate (Urokon) in quantities varying from 5 to 20 cc. and in two strengths, 35% and 70%. The larger amounts and the more concentrated solutions were used when the gall bladder was directly injected and then squeezed to fill out the extrahepatic biliary tree—the so-called cholecystocholangiogram. Larger amounts of the concentrated solution were also employed when there was a great dilatation of the ductal system, and the expected dilution of the dye with bile was correspondingly greater.

The routes and methods of injection were as follows: 1. Direct injection into the gall bladder itself. This is particularly useful when the gall bladder is normal and its removal is not anticipated, as in hepatitis or in irresectable malignant obstruction of the bile ducts. 2. Injection into the common bile duct via the cystic duct. This is the usual method when the gall bladder is present but will be removed. The cystic duct is isolated and partly divided and a fine ureteral catheter passed through the opening in the cystic duct into the common duct. Injections are then made through the catheter. 3. A single direct injection into the common duct through a short fine needle. This will be done when the gall bladder is absent or the common duct is markedly dilated. 4. The "completion cholangiogram," made by injecting the contrast medium through the catheter which is to drain the common duct, done at the conclusion of the operation.

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It is always important to avoid the injection of air bubbles (which on the film may resemble calculi). Care taken in eliminating air from syringe and catheter prior to the injection will reduce the frequency of this annoying artefact. Movement by the patient will also ruin a film; coordination between anesthetist and the x-ray technician and high-speed x-ray equipment will virtually eliminate this source of failure. Too great a concentration of the contrast medium will occasionally obscure a small calculus in the common duct; it is therefore well to obtain two films, one of which is made when the injection is half completed. This refinement is readily carried out when the injection is made through a catheter.

REPORT OF CASES

A. *Jaundice of Hepatic Origin.*—From time to time the surgeon will be called upon to explore a patient in whom every effort to elucidate the exact nature of the jaundice has failed. Frequently a hepatitis or severe cirrhosis is suspected of being the primary disease, but the medical attendants are unwilling to deny the patient the benefit of surgical relief of a possible obstruction. Often such a patient is a poor candidate for surgery, and, in addition, if he has cirrhosis, a large liver and venous collateral channels will increase technical difficulties. Yet without operative cholangiograms the surgeon will be obliged to expose the common duct and usually to explore it with instruments. A normal operative cholangiogram, on the other hand, may obviate further exploration.

CASE 1.—A woman, aged 60 years, had been suffering for six months from epigastric discomfort and anorexia. She had had several episodes of jaundice, which seemed to fluctuate in degree, and she was mildly jaundiced on admission. There had been a weight loss of 25 lb. (11.3 kg.). The liver was large, the spleen was not palpable, and there were no spider nevi. There was no roentgen evidence of esophageal varices. Laboratory data favored obstructive jaundice, although there was bile in the stool: cephalin-cholesterol flocculation, 1+; alkaline phosphatase, 38 units; albumin, 4.5 gm.; globulin, 2.8 gm. A needle biopsy of the liver showed "cirrhosis, probably biliary." At operation a normal cholecystocholangiogram (Fig. 1) ruled out extrahepatic obstruction of the bile ducts. A wedge biopsy of the liver showed biliary cirrhosis.

B. *Benign Strictures.*—An operative cholangiogram made by injecting contrast medium into the distended proximal end of an occluded common duct will establish the distance between the obstruction and the bifurcation of the right and left hepatic ducts, enabling the surgeon to plan his reconstruction with that information in mind. The operative cholangiogram finds its greatest use, however, in demonstrating an intrahepatic stricture where it would otherwise be found only by instrumentation, if at all.

CASE 2.—A woman, aged 54 years, had had a cholecystectomy in another hospital one year previously. Since that time she had experienced a number of attacks of upper abdominal pain with chills and fever. She had developed intractable itching, although she was not clinically jaundiced. At operation, a cystic duct remnant containing a small calculus was excised. The common duct itself appeared normal in size, although the wall seemed thickened. A cholangiogram was made via the cystic duct (Fig. 2), and this showed free passage of the contrast medium into the duodenum, although none appeared in the hepatic radicals, owing to an apparent block within the liver. The common duct was opened, a stricture was found at the level indicated in the cholangiogram and very gently dilated; a T-tube was introduced, and a completion cholangiogram was made. Dilatation of part of the intrahepatic ductal system was demonstrated,

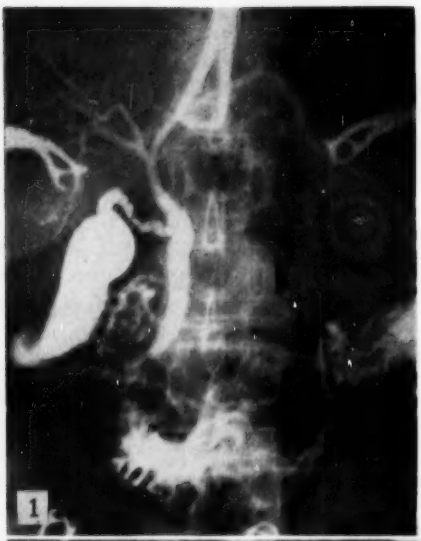

Fig. 1.—Normal cholecystocholangiogram in case of primary cirrhosis of liver.

Fig. 2.—Intrahepatic stricture of hepatic duct. *A*, arrow points to site of obstruction. *B*, completion cholangiogram after dilatation of stricture.

suggesting a block of some duration. The stricture did not appear to be related to the previous surgery. Eighteen months after this secondary operation the patient had no complaints referable to the liver and bile ducts.

Good surgical practice required an exploration of this common duct on the basis of the history, although it might have been tempting to blame all the symptoms on the diseased remnant of cystic duct. Cholangiography established an accurate diagnosis and permitted a confident dilatation of the stricture.

An operative cholangiogram will differentiate incomplete obstruction of the common duct due to stricture from such other causes as calculus, tumor, or fibrosis of the sphincter of Oddi.

CASE 3.—A woman, aged 67 years, had had two operations on the gall bladder and bile ducts in another hospital eight years before. She had her first attack of chills, fever, and jaundice a year before and had become progressively more jaundiced for the two months preceding the present hospitalization. The common duct at operation was enormously dilated, and a direct cholangiogram (Fig. 3) clearly demonstrated a stricture several centimeters above the sphincter of Oddi, confirmed by a regional biopsy showing scar tissue.

C. *Obstruction at the Sphincter of Oddi.*—Surgeons are becoming increasingly aware of the existence of pathologic states at the sphincter of Oddi due either to fibrosis at the sphincter or to narrowing from a local chronic pancreatitis. Visualization of this portion of the common duct by x-ray is essential for accurate diagnosis.

CASE 4.—A woman, aged 61 years, had had a stoneless gall bladder removed in another hospital 11 years previously. For the preceding year she had suffered from attacks of pain in the right upper quadrant of the abdomen, radiating through to the right scapula. There had been no jaundice. At operation, the common duct was somewhat dilated, and the operative cholangiogram (Fig. 4) showed narrowing of the distal centimeter of the common duct. This was apparently due to a regional pancreatitis. A transduodenal sphincterotomy was carried out, and the patient was still free of symptoms one year later.

Sometimes the operative cholangiogram will expedite a pancreaticoduodenectomy for malignant disease by outlining a tumor at the ampulla of Vater.

CASE 5.—A man, aged 60 years, had been intensely jaundiced for several months. Cholecystectomy performed at another hospital two months earlier had failed to improve his condition. At operation, cholangiograms showed a tumor of the ampulla of Vater (Fig. 5) which proved to be a resectable carcinoma about 2 cm. in greatest diameter. The patient remained well for three years, when a recurrence was proved at another operation.

D. *Obstruction by Extrinsic Malignant Disease.*—The diagnosis of carcinoma of the pancreas, gall bladder, or bile ducts (excluding the hidden lesions in the region of the ampulla of Vater exemplified by Case 5) will normally be made by direct observation at the time of surgery and confirmed by biopsy. Operative cholangiograms may be very useful, however, if the lesion is not resectable and a procedure is contemplated for shunting the bile around the obstruction.

CASE 6.—A man, aged 70 years, had suffered from progressive jaundice over a period of six weeks. At operation he proved to have a carcinoma of the head of the pancreas with liver metastases. A cholecystocholangiogram (Fig. 6) showed a long cystic duct entering the common duct very near the site of obstruction. A cholecystenterostomy, ordinarily the palliative operation of choice, would have been ill advised under these circumstances, since the cystic duct would soon have been shut off by advancing cancer. Instead, the common duct was anastomosed to the duodenum at a point well above the obstruction. The patient lived for a year after this operation, and remained free of jaundice.

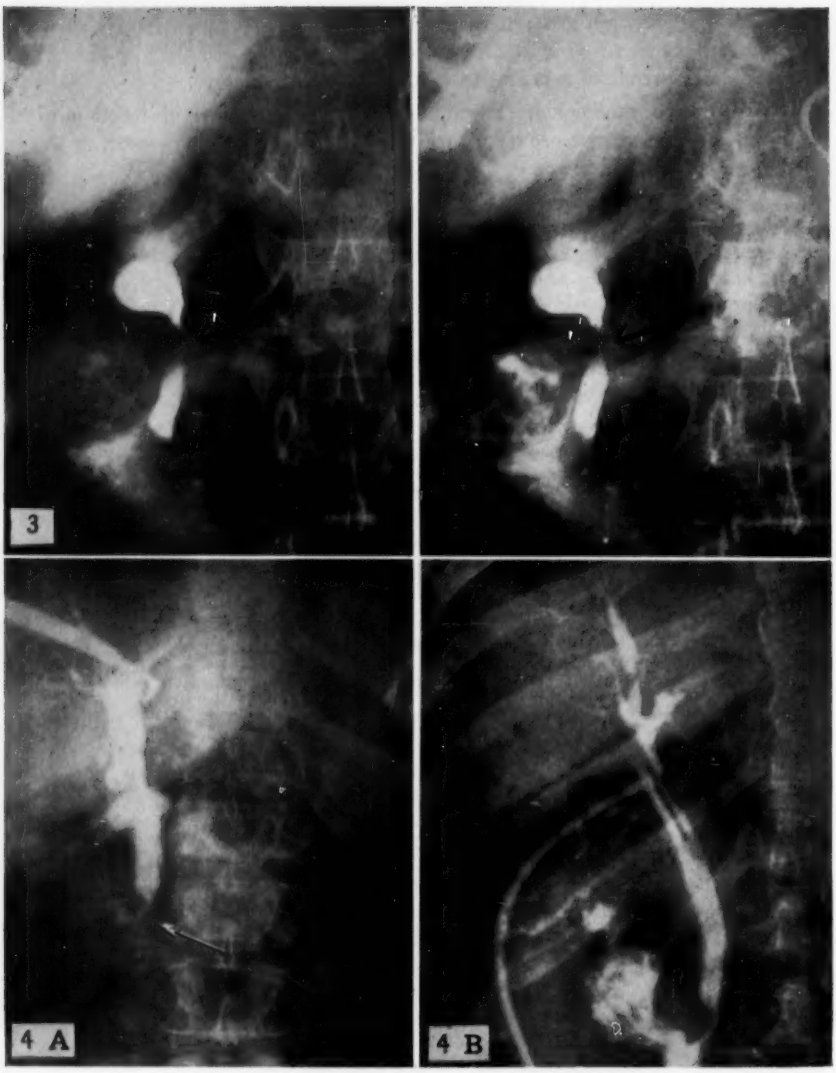

Fig. 3.—Benign stricture of common duct with incomplete obstruction.

Fig. 4.—Narrowing of distal common duct from chronic pancreatitis. *A*, arrow points to narrowed region. *B*, Postoperative cholangiogram after transduodenal sphincterotomy.

A laborious dissection would have been required in this case to establish the pertinent anatomical facts if a cholangiogram had not been available.

CASE 7.—A jaundiced man, aged 66 years, proved to have a cancer of the bile ducts at the porta of the liver. A cholecystocholangiogram made at the first operation (Fig. 7*A*) showed contrast medium entering the duodenum. This made it clear that the obstruction lay above

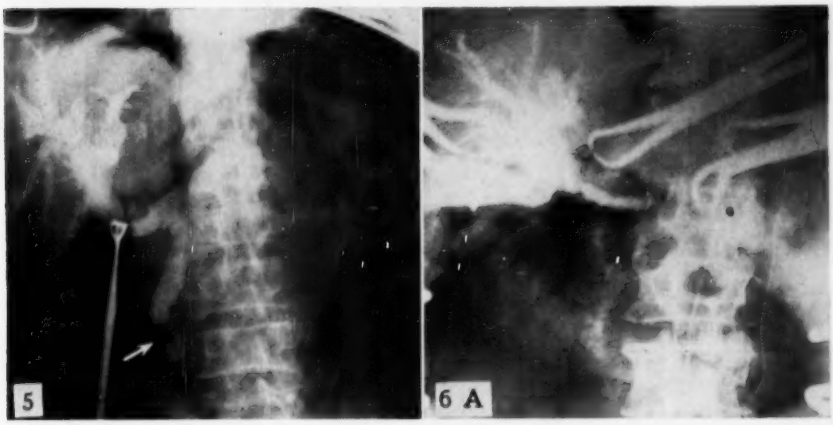

Fig. 5.—Carcinoma of ampulla of Vater.

Fig. 6*A*.—Obstruction of common duct from carcinoma of head of pancreas. Cholecystocholangiogram shows very long cystic duct.

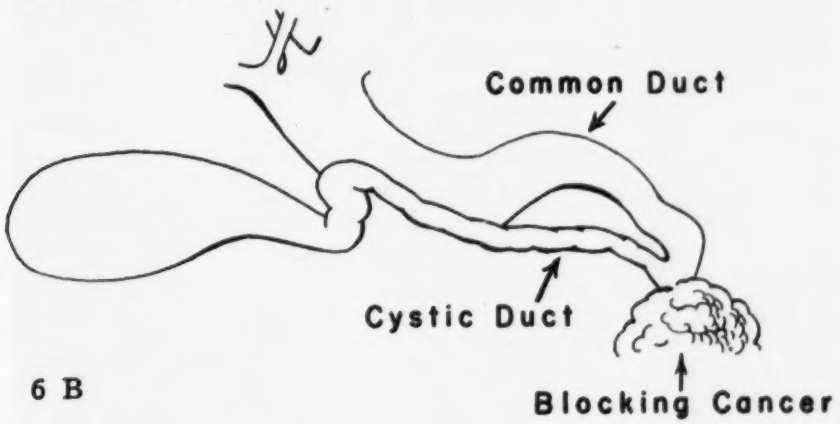

Fig. 6*B*.—Diagrammatic representation of x-ray (Fig. 6*A*) demonstrating why cholecystenterostomy would not be beneficial.

the cystic duct and that a cholecystenterostomy would be futile. No procedure beyond a biopsy was carried out at this time, but several months later, at the insistence of the patient (who was aware of the hopeless nature of his disease), a second operation was performed in an effort to establish a bypass for the bile. A small segment of the right lobe of the liver was excised, one of the small ducts appearing on this cut surface forcibly dilated, a catheter introduced, and a cholangiogram made (Fig. 7*B*). The x-ray showed that the superficial duct had wide communi-

cations within the liver. An anastomosis was constructed between this duct and the jejunum, and an effective decompression of this portion of the biliary tract with diversion of the bile into the intestine was demonstrated in the postoperative cholangiogram (Fig. 7*C*). The patient lived only two months after this second operation, but he had relief from his intolerable itching.

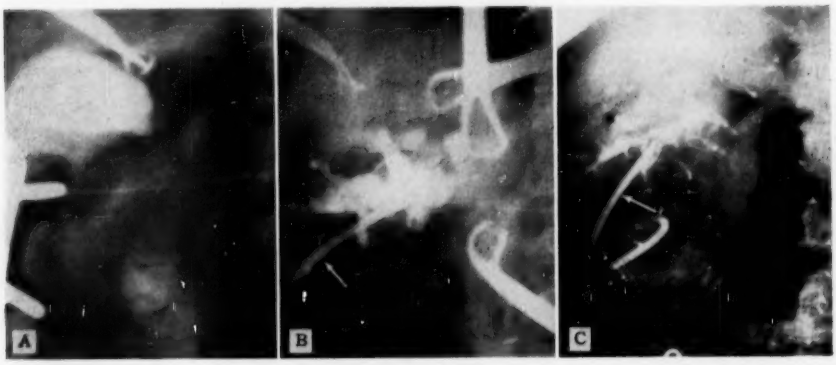

Fig. 7.—Carcinoma of bile ducts with obstruction above cystic duct. *A*, cholecystocholangiogram showing contrast medium in duodenum. *B*, cholangiogram at second operation. Contrast medium introduced through catheter in duct on cut surface of liver. Arrow points to catheter. *C*, postoperative cholangiogram showing decompression of hepatic ducts and contrast medium in jejunum. Arrow points to long limb of T-tube.

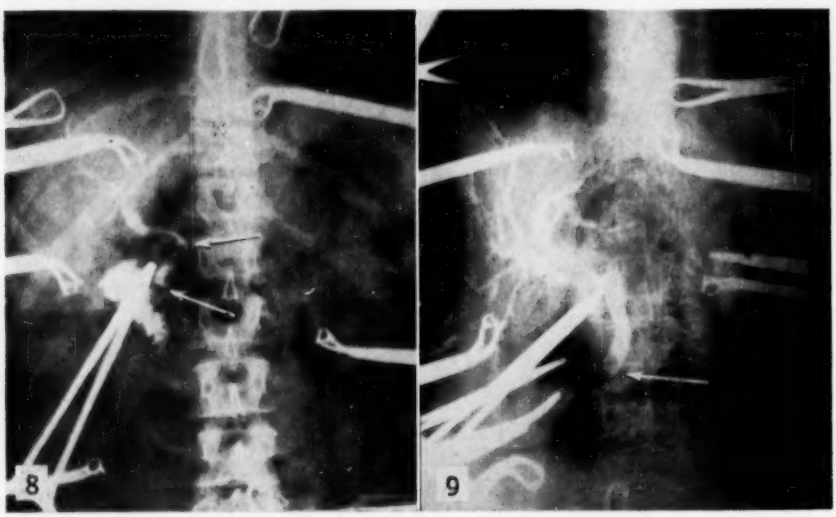

Fig. 8.—Routine operative cholangiogram showing two unsuspected stones in common bile duct.

Fig. 9.—Routine operative cholangiogram showing single stone in common bile duct.

E. *Common Duct Calculi.*—Routine operative cholangiography may be regarded as a preventive measure against future obstruction and jaundice when it discloses unsuspected stones in the common bile duct.

CASE 8.—A woman, aged 37 years, had for six months experienced a burning sensation in the right upper quadrant of the abdomen, appearing one to three hours after meals and relieved by eating. When oral cholecystograms demonstrated gallstones, cholecystectomy was advised more as a prophylactic measure to avoid future trouble than as a means of relieving serious existing symptoms. There had never been any colic or jaundice. At operation, the common duct and the cystic duct seemed normal, but a routine operative cholangiogram (Fig. 8) showed two stones in the common duct. These were easily removed.

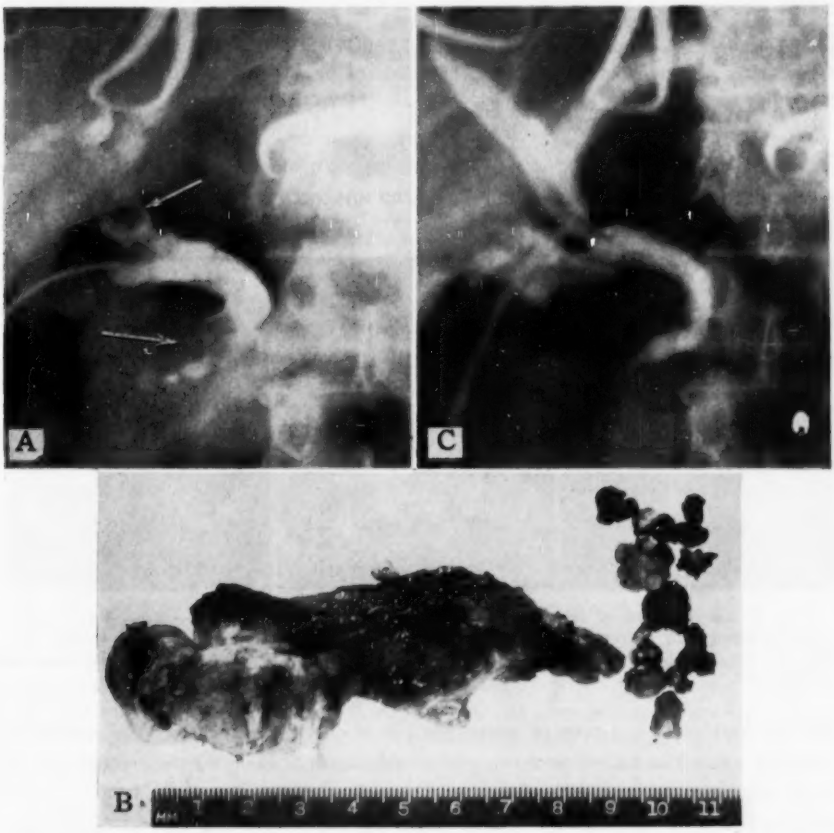

Fig. 10.—Multiple stones in common bile duct. *A*, operative cholangiogram with arrows pointing to two irregular filling defects. *B*, photograph of gall bladder with variety of common duct stones to right. *C*, completion cholangiogram showing no filling defects.

Even when the surgeon is quite sure that he must be dealing with stones in the common duct, cholangiography may facilitate the operation by disclosing the number, size, and location of the stones.

CASE 9.—A woman, aged 72 years, with moderate hypertension, had a cholecystectomy for recurrent bouts of gallstone colic without jaundice. At operation the common duct was found to be dilated and evidently required exploration. A routine cholangiogram was made (Fig. 9) and revealed a single large calculus at the distal end of the common duct. While the x-ray

film was being developed (a process which rarely exceeds 10 minutes), the common duct was opened. The offending stone was not found, however, until the film was seen, after which its extraction was easy.

When there are multiple stones in the common duct, the surgeon must always worry lest he leave some behind. No matter how thorough the scooping and irrigations, a satisfactory completion cholangiogram gives additional assurance that no calculi remain to cause trouble in the future.

CASE 10.—A man, aged 46 years, had suffered for two years from recurrent attacks of abdominal pain accompanied by chills, fever, and jaundice. At operation, numerous stones of various sizes were recovered from a large common duct (Fig. 10). A completion cholangiogram showed no negative shadows and gave additional assurance that the duct was free from residual calculi.

F. *Miscellaneous Conditions.*—The routine use of operative cholangiography in surgery of the bile ducts occasionally yields an unexpected dividend. The following

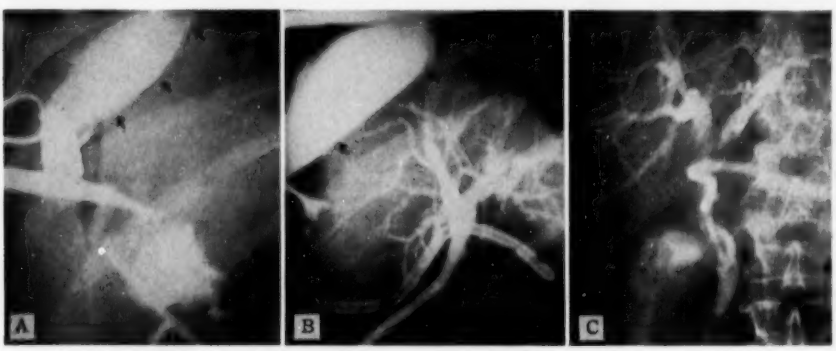

Fig. 11.—*A*, injection of supposed common duct "cyst" with contrast medium, showing dye in right subphrenic space. *B*, proximal end of common duct communicating with cyst and injected via catheter. *C*, postoperative cholangiogram showing end-to-end anastomosis of divided duct.

case is cited as an example in which the life of the patient was in all probability saved as a result of a routine x-ray, and a serious surgical blunder corrected before it did any harm.

CASE 11.—A jaundiced woman, aged 62 years, had had a cholecystectomy performed nine months previously in another hospital. All went well for several months, and then she began to itch; frank jaundice developed a month before her second operation. It was presumed that she had a calculus in the common duct. At the secondary operation a cyst was found, about 10 cm. in diameter and containing bile, with a membrane-like lining. At this point it was decided that the patient had a true cyst of the common duct, and further exploration was abandoned, both because the patient was elderly and obese and because there were many bloody adhesions within the abdomen. An anastomosis was constructed between the cyst and the nearby duodenum; a T-tube was placed across the anastomosis, and almost as an afterthought a completion cholangiogram was made (Fig. 11). This showed that the contrast medium had accumulated beneath the right diaphragm! It became obvious that the "cyst" was in reality a bile collection with a fibrous wall and that the "anastomosis" connected the duodenum directly to the subphrenic space! As a direct result of this x-ray, the duodenum was closed, the "cyst" explored, its connection

with a completely divided common duct demonstrated, and the upper and lower ends of the common duct dissected out and united with an end-to-end anastomosis. When last seen, 21 months after this operation, the patient was in comparatively good health and free of jaundice —a state she owed directly to the operative cholangiogram.

SUMMARY AND CONCLUSIONS

Operative cholangiograms have a wide field of usefulness when the surgeon employs them during surgery on jaundiced patients. They may demonstrate completely normal ducts (when the jaundice is of hepatic origin) or may show the location and nature of benign or malignant obstructions. Illustrative cases are presented.

DISCUSSION

DR. PHILIP F. PARTINGTON, Cleveland: I am very happy to have the opportunity to discuss this interesting paper by Dr. Hoerr. Certainly anyone who has had experience with cases that are trying, such as the ones he has described, and who has tried cholangiography, I think, will find the procedure feasible.

The most important thing about cholangiography, in my opinion, is its routine use. As seen from Dr. Hoerr's case in which the common duct stones were unsuspected, it is impossible to select the proper cases on which to do cholangiography. If the procedure is not done routinely, the operating-room setup is not adequate, the nurses do not expect it, the equipment is not there, and one ends up not doing the operation.

Just a few other points about technique: I think it is important to rotate the patient right side down about 14 degrees to throw the bile ducts away from the spine. Sometimes the bony detail of the spine will confuse you.

As Dr. Hoerr has said, the most foolproof method is a catheter inserted through the cystic duct stump. It is important not to insert it over 5 cm., otherwise you are likely to find it in the duodenum. It also is important to ligate the duct around the catheter so that there is no leakage of dye.

There is a group of cases, however, in which the gall bladder is absent or in which the gall bladder is normal and the common duct dilated, and it is therefore necessary to put the dye in through a needle. Obviously, if it is not certain whether the gall bladder is going to be needed for a sidetracking procedure, no hole should be cut in the cystic duct.

We prefer to use a small hypodermic needle attached to amber rubber tubing so that the needle can be inserted into the common duct and left in place for serial films, serial injections of 5 cc. of contrast medium, and the exposure of three films.

It has been our practice to use dilute dye for the dilated common duct for the reason that you can lose small stones in big ducts if you use 70% iodopyracet (Diodrast). If the stone is not touching the wall of the duct, it may be completely surrounded by contrast medium and thus lost.

I want to demonstrate an alternative method to the two mentioned for injecting the contrast medium and present a couple of cases that illustrate it. The first case was that of a 68-year-old man with painless jaundice of two weeks' duration. He had no chills and no fever. He had the chemistry of obstructive jaundice. He had a mass which was thought to be a metastasis in his liver, and the preoperative diagnosis was carcinoma, probably metastatic to the liver.

When the abdomen was opened, the gall bladder was found to be acutely inflamed and to contain pus. There were nodules in the liver, but they looked like abscesses. We searched diligently for the common duct but could not find it, and so we made use of an alternative method of injecting the iodopyracet.

[Slide] This consisted of inserting a 3 in. (7.6 cm.), No. 22 gauge needle through the liver substance until we found a large duct, aspirated white bile from it, and injected the iodopyracet. Here you can see why the gall bladder is full of pus—at least that the cystic duct is completely obstructed. This is the only communcation between the common hepatic or the junction of the hepatic ducts and the common duct—that little narrow tract there.

[Slide] We then injected the gall bladder just to demonstrate that it did not communicate. Here again you can see the narrow area in the duct system, and the dye entering the duodenum.

We obtained a biopsy specimen of the liver, and the pathologist told us it was inflammatory.

[Slide] Here, however, is the specimen at autopsy. This man did have a carcinoma which had constricted the hepatic ducts up in the liver.

[Slide] The second case is similar, that of a man of the same age, with one month of obstructive jaundice. Upon exploration he did have nodules in his liver that were obviously carcinoma, but this cholangiogram performed through a needle inserted through liver parenchyma at least demonstrated that there were no ducts in the left lobe of the liver accessible for a Longmire procedure in that area.

I have enjoyed this paper very much, and I hope it will stimulate others to use operative cholangiography.

DR. JOHN ARMES GIUS, Iowa City: I have enjoyed Dr. Hoerr's paper. He has called our attention to a very important aspect in hepatic and biliary-tract surgery.

With your permission, I should like to show an alternative technique for cholangiography which was suggested by Dr. Robert Hickey, of our staff, and which we have utilized at the University of Iowa since July, 1953. This method simplifies the technical details, prevents contamination and delay of operation, and makes unnecessary the moving of heavy radiographic equipment during operation.

[Slide] In this particular method of cholangiography the arm of the portable x-ray machine is placed beneath the table at the head of the table (opposite the anesthetic machine), with the tube directed upward.

[Slide] There is an opening between the footpiece and the body of the operating table. We use the American Sterilizer type of table, which has a large aperture. We cover the opening with either a board or a plastic covering and pad it sufficiently so that the patient is comfortable on the table.

The equipment is all set up before the operative procedure is undertaken. The patient is positioned so that the biliary tract is centered over the aperture. A scout film is taken at that time, and no movement of the equipment is necessary after this arrangement.

[Slide] Two standard types of films are taken. One is an intra-abdominal film, of which this is a reproduction. This is a small film in a kidney cassette and is contained in a sterile rubber envelope which is placed over the anterior duodenal wall in close proximity to the common bile ducts and pancreatic ducts and gives very clear and precise definition of these structures.

A larger film in a grid cassette and contained in a sterile pillowcase is placed over the anterior abdominal wall, and the exposures are made of the entire duct system.

We ordinarily use 10 cc. of 35% iodopyracet for the first exposure and take the second exposure after injecting 5 to 10 cc. more.

DR. RUDOLF J. NOER, Louisville: I have enjoyed the discussion and the paper very much indeed. I am impelled to arise for additional discussion only because of a remark I heard made outside of a meeting three or four months ago, to the effect, "We don't do operative cholangiograms because we don't have the equipment for it."

At the University of Louisville we are still eagerly awaiting a new operating suite in which we hope there will be fine, built-in radiographic equipment. However, with a portable Bucky diaphragm and a mobile unit, and, as Dr. Hoerr said, a cheerful x-ray department, we get a great deal of help from the procedure of operative cholangiography with only the equipment that is available to almost everybody. It is an extremely valuable procedure and one that I think should be much more widely used.

DR. STANLEY O. HOERR, Cleveland: I should like to say a word about what I believe to be the place of operative cholangiography.

A "normal" cholangiogram is not a contraindication to an exploration of the common duct if there are sound clinical reasons for such an exploration. I do not hesitate to open the common duct under such circumstances and several times have recovered small stones which had not appeared on the x-rays. Operative cholangiography is no substitute for a clinical appraisal before and during the operation, but it is a very valuable supplement.

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SCIENTIFIC EXHIBITS

Beginning with the October, 1954, issue the department "Scientific Exhibits" will be a frequent feature of the A. M. A. ARCHIVES OF SURGERY. This feature attempts to preserve in more permanent form some of the instructive Scientific Exhibits that are presented at the Annual Meetings of the American Medical Association. Although thousands of physicians attend the Annual Meetings, viewing and studying the scientific exhibits at first hand, other thousands are unable to attend. For the first time, the latter group is now given the opportunity to see the exhibits reproduced in the pages of the various A. M. A. Specialty Journals.

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CORRECTION

Throughout the article by Drs. Max S. Sadove, Gordon M. Wyant, and Gwen Gleave, on pages 779-786 in the June, 1954, issue of the A. M. A. Archives of Surgery, a misprint appeared in the Council-accepted generic name for Arfonad. The proper term should be trimethaphan camphorsulfonate.

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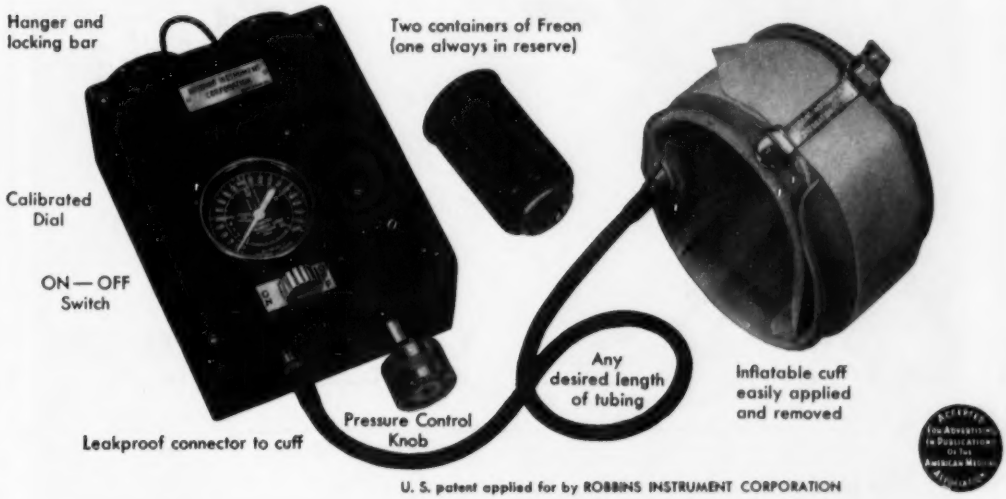
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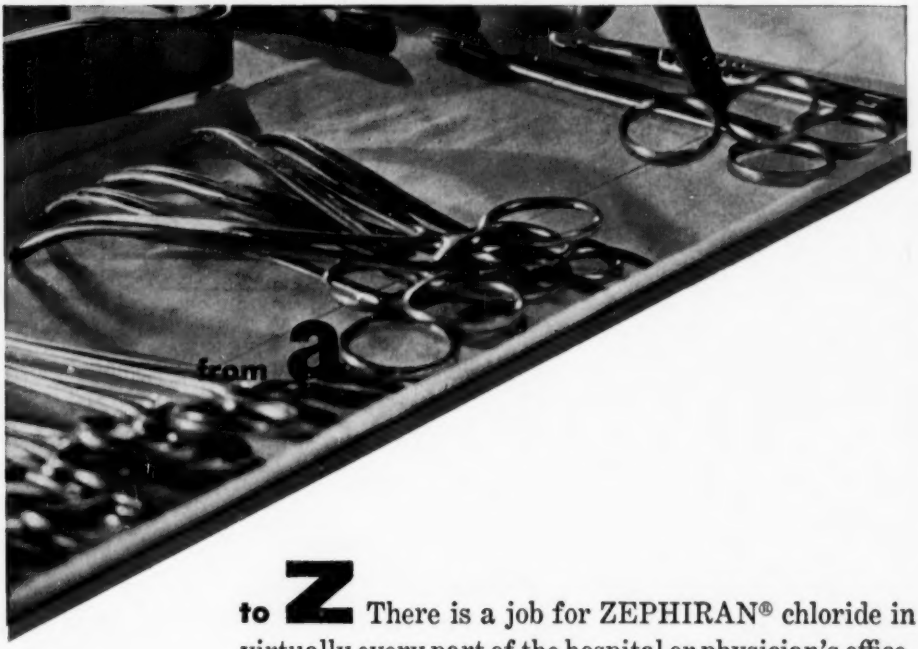

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